AGENTS FOR IMPROVING EXCRETORY POTENCY OF URINARY BLADDER

Technical Field

The present invention relates to drugs, particularly agents for improving excretory potency of the urinary bladder.

Background Art

Inferior uropathy is a general term for subjective or objective disorders in a process through accumulation of urine (urinary storage) till excretion (urination), which may be classified into urinary cumulative disorders (incontinence of urine, pollakiuria, etc.), dysuria (difficulty of urination, scalding, obstruction of urinary tract, etc.), and the like. The inferior uropathy in the aged, particularly dysuria, especially dysuria caused by prostatomegaly, becomes a great problem of public concern with the advance of a recent aging society, though the inferior uropathy may also be found in the youth.

Urination is, under the control of the urination center, controlled by the peripheral nervous system involving a parasympathetic nerve such as pelvic nerve, sympathetic nerve such as hypogastric nerve, and somatic nerve such as pudendal nerve, and it is suggested that a

variety of neurotransmitters (e.g., acetylcholine, adrenaline, ATP, Substance P, neuropeptide Y, etc.) are involved in urination.

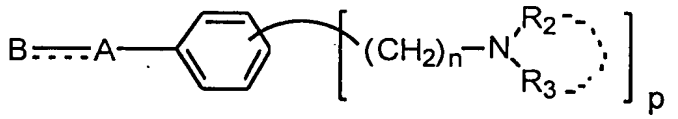
As agents for treatment of dysuria, particularly difficulty of urination, those for increasing contraction of muscle of urinary bladder (detrusor) or relaxing sphincter muscle of urethra to reduce urethral resistance have been used. As the agents acting on the muscle of urinary bladder to increase the contraction, for example, cholinergic agents such as bethanechol, acetylcholinesterase inhibitors such as distigmine, and the like have been used. For example, bethanechol however is incompatible with pregnant women, peptic ulcers, organic ileus, asthma, hyperthyroidism, etc., because it has adverse effects such as epiphora, sweating, gastro-intestinal disorders, stomachache, etc. No satisfied drugs have yet been found.

As the acetylcholinesterase inhibitors increasing contraction of muscle of urinary bladder, carbamate- type acetylcholinesterase inhibitors having a carbamate structure (-OCON-) in its molecule (e.g., distigmine, neostigmine, etc.) are known. Said carbamate-type acetylcholinesterase inhibitors are known to express the inhibitory effect based on the carbamate structure which is characteristics of the molecule (Goodman & Gilman's The

PHARMACOLOGICAL BASIS OF THERAPEUTICS, Ninth ed., McGraw-Hill, New York, p. 161-176). However, it is known that, for example, distigmine is insufficient in its clinical efficacy since it contracts the muscle of urinary bladder with constriction of the muscle of urethra to increase urethral resistance and consequently make the voiding flow rate worse. In addition, neostigmine has not been used in therapy because of short duration of the action (Takamichi Hattori and Kosaku Yasuda, " Sinkeiinseiboukou-No-Sindan-To-Chiryou (Diagnosis and Therapy of Neurogenic Bladder)", 2nd Ed., p. 105-106, p. 139, Igaku-Shoin Ltd. Tokyo).

On the other hand, a variety of amine compounds which have an acetylcholinesterase inhibiting effect and are different from carbamate-type inhibitors in their structure have been reported as follows.

(1) Compounds of the following formula:



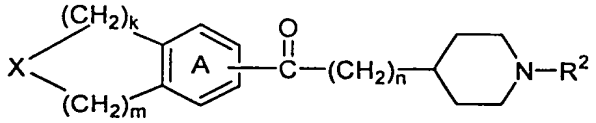
wherein B represents an optionally substituted saturated or unsaturated 5- to 7-membered aza-heterocyclic group; A is a bonding or alkylene or alkenylene optionally substituted with hydrocarbon residue, oxo or hydroxy; --- indicates a single bond or double bond (where when A is a bonding, --- indicates a single bond); R_2 and R_3 each represents independently hydrogen or optionally substituted

hydrocarbon residue (but they are not hydrogen concurrently) or they may be taken with the adjacent nitrogen atom to form a cyclic amino group; n indicates 0, 1 or 2; and p indicates 1 or 2;

or salts thereof as described in EP-A-0 378 207.

Such compounds as described are exemplified by 3-[1-(phenylmethyl)piperidin-4-yl]-1-[4-(pyrrolidin-1-yl)phenyl]-1-propanone, 1-[4-(N,N-dimethylamino)phenyl]-3-[1-(phenylmethyl)piperidin-4-yl]-1-propanone, and the like.

(2) Compounds of the following formula:



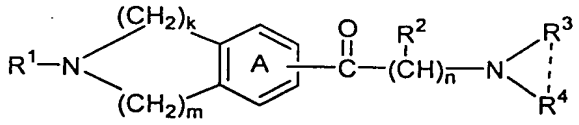
wherein X represents R^1-N< (R^1 is hydrogen, optionally substituted hydrocarbon group or optionally substituted acyl), oxygen or sulfur; R^2 represents hydrogen or optionally substituted hydrocarbon group; the ring A represents an optionally substituted benzene ring; k indicates an integer of 0-3; m indicates an integer of 1-8; and n indicates an integer of 1-6;

or salts thereof as described in Japanese Patent Unexamined Publication No. (hereinafter referred to as JP-A) 5-140149/1993.

Such compounds as described are exemplified by 3-[1-(phenylmethyl)piperidin-4-yl]-1-(2,3-dihydro-1H-indol-5-yl)-1-propanone, 3-[1-(phenylmethyl)piperidin-4-yl]-1-

(2,3,4,5-tetrahydro-1H-1-benzazepin-8-yl)-1-propanone, and the like.

(3) Compounds of the following formula:

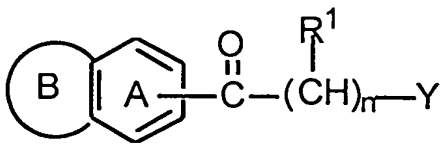


wherein R^1 represents hydrogen, optionally substituted hydrocarbon group or optionally substituted acyl; the ring A represents an optionally further substituted benzene ring; n is an integer of 1 to 10; R^2, R^3 and R^4 are the same or different representing hydrogen or optionally substituted hydrocarbon group, or R^3 and R^4 may be taken with the adjacent nitrogen atom to form an optionally substituted heterocyclic group, and R^2 may be different respectively according to repetition of n; k is an integer of 0 to 3; m is an integer of 1 to 8; provided that when k=0 and m=2, then n>1;

or salts thereof as described in JP-A 6-166676/1994.

Such compounds as described are exemplified by 3-[1-(phenylmethyl)-2,3,4,5-tetrahydro-1H-3-benzazepin-7-yl]-3-[4-(phenylmethyl)piperazin-1-yl]-1-propanone, 1-[2-(phenylmethyl)-2,3,4,5-tetrahydro-1H-2-benzazepin-8-yl]-3-[4-(phenylmethyl)piperazin-1-yl]-1-propanone, and the like.

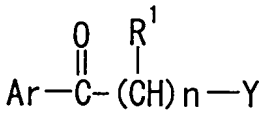
(4) Compounds of the following formula:



wherein the ring A represents an optionally further substituted benzene ring; the ring B represents an optionally substituted non-aromatic heterocyclic ring containing the same or different, two or more hetero atoms; R^1 represents hydrogen or optionally substituted hydrocarbon group, which may be different according to repetition of n; Y represents an optionally substituted amino or optionally substituted nitrogen-containing saturated heterocycle; and n is an integer of 1 to 10; or salts thereof as described in JP-A 6-206875/1994.

Such compounds as described are exemplified by 3-[1-(phenylmethyl)piperidin-4-yl]-1-(2,3,4,5-tetrahydro-1,4-benzoxazepin-7-yl]-1-propanone and the like.

(5) JP-A 7-206854/1995 discloses the formula:

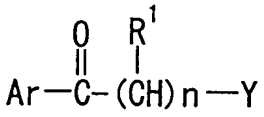


wherein Ar represents an optionally substituted tricyclic condensed benzene ring group condensed with at least one heterocycle; n is an integer of 2 to 10; R^1 represents hydrogen or optionally substituted hydrocarbon group, which may be different according to repetition of n; Y represents 4-piperidinyl, 1-piperadinyl or 4-benzyl-1-piperidinyl,

each of which may have a substituent or substituents.

Such compounds as described are exemplified by 8-[3-[1-(phenylmethyl)-4-piperidinyl]-1-oxopropyl]-1,2,5,6-tetrahydro-4H-pyrrolo[3,2,1-ij]quinolin-4-one, 1-(1,2,2a,3,4,5-hexahydrobenz[cd]indol-6-yl)-3-[1-(phenylmethyl)-4-piperidinyl]-1-propanone, and the like.

(6) Compounds of the following formula:



wherein Ar represents an optionally substituted tetracyclic condensed heterocyclic group; n is an integer of 1 to 10; R^1 represents hydrogen or optionally substituted hydrocarbon group, which may be different according to repetition of n; Y represents an amino or nitrogen-containing saturated heterocyclic group, each of which may have a substituent or substituents;
or salts thereof as described in JP-A 7-309835/1995.

Such compounds as described are exemplified by 3-[3-[1-(phenylmethyl)-4-piperidinyl]-1-oxopropyl]-7,11b,12,13-tetrahydro-5H-isoindolo[2,1-b][2]benzazepin-7-one, 2-[1-oxo-3-[1-(phenylmethyl)-4-piperidinyl]-4,5,7a,8,9,10,11,11a-octahydro-6H-pyrido[3,2,1-jk]carbazol-6-one, and the like.

(7) Amine compounds described in WO 93/07140, PCT Japanese Patent Unexamined Publication No. (hereinafter

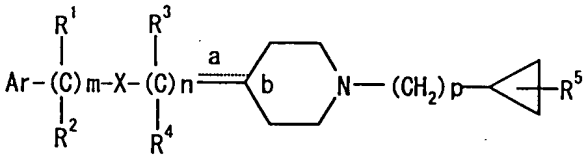
referred to as PCT JP-A) 6-500794/1994, JP-A 4-234845/1992, JP-A 6-116237/1994, JP-A 7-109275/1995, WO 97/37992, JP-A 5-148228/1993, JP-A 5-194359/1993, JP-A 6-507387/1994, PCT JP-A 7-502272/1995, PCT JP-A 8-511515/1996, JP-A 6-41070/1994, JP-A 5-9188/1993, JP-A 5-279355/1993, JP-A 5-320160/1993, JP-A 6-41125/1994, JP-A 5-345772/1993, JP-A 7-502529/1995, JP-A 64-79151/1989, JP-A 62-234065/1987, JP-A 4-235161/1992, JP-A 4-21670/1992, JP-A 9-268176/1997, and so on.

(8) Amine compounds described in JP-A 2-167267/1990, JP-A 63-166881/1988, JP-A 2-96580/1990, JP-A 3-153667/1991, JP-A 61-148154/1986, Japanese Patent Examined Patent No. (hereinafter referred to as JP-B) 5-41141/1993, JP-A 63-284175/1988, JP-A 3-95161/1991, JP-A 3-220189/1991, JP-A 4-134083/1992, JP-A 4-66571/1992, PCT JP-A 11-500144/1999, PCT JP-A 10-511651/1998, JP-A 4-290872/1992, JP-A 2-231421/1990, JP-A 4-18071/1992, JP-A 4-159225/1992, JP-A 4-346975/1992, WO 99/11625, J. Am. Chem. Soc., 1991, 113, p. 4695-4696, J. Am. Chem. Soc., 1989, 111, p. 4116-4117, WO 97/11077, Heterocycles, 1977, 8, p. 277-282, J. Chem. Soc. (C), 1971, p. 1043-1047, and so on.

(9) Amine compounds described in JP-A 2-91052/1990, JP-A 3-95143/1991, JP-A 3-141244/1991, JP-A 3-223251/1991, JP-A 5-239024/1993, JP-A 2-138255/1990, and so on.

Moreover, amine compounds having various pharmacological actions have been reported as follows.

(1) WO 91/03243 describes compounds of the following formula:

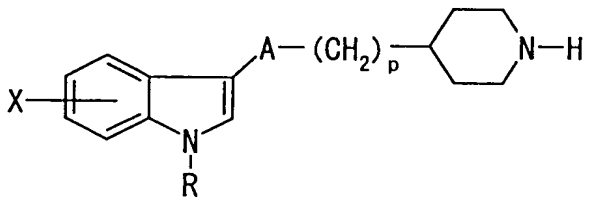


wherein m is 0 to 3, n is 0 to 3, and m and n are not 0 at the same time; p is 0 to 3; X is O, S, SO, SO_2, NR^6, CR^7R^8, CO or CHOH; R^1, R^3 and R^7 each represents hydrogen, C_{1-5} alkyl, halogen, $NR^{10}R^{11}$, OH, COOH, C_{2-6} carbalkoxy, CN, Ar, C_{1-5} alkoxy or C_{1-5} alkylthio; R^2, R^4 and R^8 each represents hydrogen, C_{1-5} alkyl, C_{2-6} carbalkoxy, CN, C_{1-5} alkoxy or Ar^1; when X is O, S, SO, SO_2 or NR^6, then R^1, R^2, R^3 and R^4 are not C_{1-5} alkoxy, C_{1-5} alkylthio, $NR^{10}R^{11}$ or OH; R^5 represents hydrogen, alkyl, halogen, OH or alkenyl; R^6 represents hydrogen, C_{1-5} alkyl or Ar^1; Ar and Ar^1 each represents naphthyl, pyridyl, pyrimidyl, indolyl, quinolinyl, isoquinolinyl or phenyl, and these groups may be substituted by C_{1-3} alkyl, C_{1-3} alkoxy, C_{1-3} haloalkyl containing 1 to 7 halogen atoms, SH, S(O)t-C_{1-3} alkyl (t is 1, 2 or 3), C_{2-6} dialkylamino, halogen, C_{1-3} alkylamino, NH_2, CN, NO_2, SO_3H, tetrazole, COOH, C_{2-6} carboalkoxy, $CONH_2$, SO_2, NO_2, COR^9, $CONR^{12}R^{13}$, $SO_2NR^{12}R^{13}$, Ar^2, OAr^2 or SAr^2; Ar^2 is naphthyl or phenyl, and these groups may be substituted by

C_{1-3} alkyl, C_{1-3} haloalkyl containing 1 to 7 halogen atoms, C_{1-3} alkoxy, halogen or C_{1-3} alkylthio; R^9, R^{10}, R^{11}, R^{12} and R^{13} each represents hydrogen, C_{1-5} alkyl or phenyl, R^{10} and R^{11} together may form a C_{3-6} alkylene chain, R^{12} and R^{13} together may form a C_{3-6} alkylene chain; a or b indicates a double bond or single bond, but they are not double bond at the same time;

or pharmacologically acceptable salts thereof which can be used as antipsychotics.

(2) JP-A 52-72829/1977 describes compounds of the following formula:



wherein R is hydrogen, alkyl containing 1 to 4 carbon atoms, or aralkyl of which the alkyl portion contains 1 or 2 carbon atoms; X is hydrogen or halogen, alkyl, alkoxy or alkylthio, each of which may contain 1 to 4 carbon atoms, trifluoromethyl, nitro, hydroxy or unsubstituted amino, or amino substituted by 1 or 2 alkyl groups or acyl or alkylsulfonyl; A is a group -CO- or $-CH_2-$; and n is 0, 1 or 2;

or salts thereof which can be used in treatment of diseases caused particularly by serotonergic dysfunction.

In these compounds, however, there is neither report nor suggestion nor disclosure on the effect as prophylactics or therapeutic agents for dysuria (difficulty of urination) or on the effect as excretion improving agents for the urinary bladder, until now.

Therefore, it has been desired to develop prophylactics or therapeutic agents for dysuria, particularly difficulty of urination, which have high efficiency for urination and high versatility compared with known compounds which are known to have an effect improving excretion of the urinary bladder.

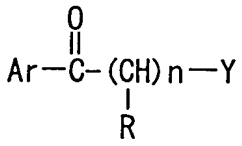
Disclosure of the Invention

In view of such current realities, the present inventors started a research for highly effective new agents for improving excretion of the urinary bladder with high efficiency of urination, that is, therapeutic agents for dysuria, particularly for difficulty of urination. As a result of diligent investigation, they have discovered that acetylcholinesterase-inhibiting amine compounds of non-carbamate-type show an unexpectedly high effect of improving excretion of the urinary bladder as well as prophylactic or therapeutic effect for dysuria, particularly for difficulty of urination with an unexpectedly high effect of increasing the contraction

potency of the muscle of urinary bladder but no effect of contracting the muscle of urethra. The invention was completed based on these findings. That is, the present invention relates to:

(1) An agent for improving excretory potency of the urinary bladder which comprises an amine compound of non-carbamate-type having an acetylcholinesterase-inhibiting action,

(2) An agent as described in the above item (1), wherein the amine compound is a non-carbamate-type compound of the formula:



wherein Ar is optionally condensed phenyl in which the phenyl moiety may be substituted by a substituent or substituents;

n is an integer of 1 to 10;

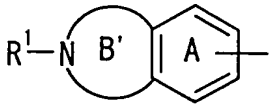
R is hydrogen or optionally substituted hydrocarbon group;

Y is optionally substituted amino or optionally substituted nitrogen-containing saturated heterocyclic group;

or a salt thereof,

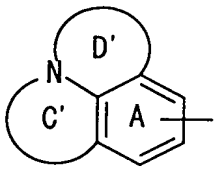
(3) An agent as described in the above item (2),

wherein Ar is a group of the formula:



wherein R^1 is hydrogen, optionally substituted hydrocarbon group, acyl, or optionally substituted heterocyclic group; the ring A is an optionally substituted benzene ring; the ring B' is a 5- to 9-membered nitrogen-containing heterocycle which may further be substituted by oxo,

(4) An agent as described in the above item (2), wherein Ar is a group of the formula:

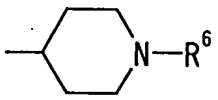


wherein the ring A is an optionally substituted benzene ring; the rings C' and D' each is a 5- to 9-membered nitrogen-containing heterocycle which may further be substituted by oxo,

(5) An agent as described in the above item (2), wherein n is 2,

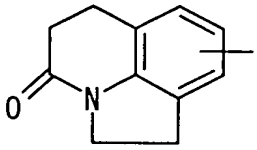
(6) An agent as described in the above item (2), wherein R is hydrogen,

(7) An agent as described in the above item (2), wherein Y is a group of the formula:

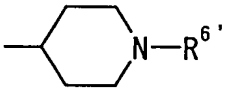


wherein R^6 is hydrogen, optionally substituted hydrocarbon group, acyl, or optionally substituted heterocyclic group;

(8) An agent as described in the above item (2), wherein Ar is a group of the formula:



n is 2; R is hydrogen; and Y is a group of the formula:



wherein $R^{6'}$ is benzyl which may be substituted by 1 or 2 substituents selected from halogen, C_{1-3} alkyl, C_{1-3} alkoxy, cyano, nitro and hydroxy;

(9) An agent as described in the above item (1) comprising 8-[3-[1-[(3-fluorophenyl)methyl]-4-piperidinyl]-1-oxopropyl]-1,2,5,6-tetrahydro-4H-pyrrolo[3,2,1-ij]quinolin-4-one,

8-[3-[1-(phenylmethyl)-4-piperidinyl]-1-oxopropyl]-1,2,5,6-tetrahydro-4H-pyrrolo[3,2,1-ij]quinolin-4-one,

8-[3-[1-[(2-hydroxyphenyl)methyl]-4-piperidinyl]-1-oxopropyl]-1,2,5,6-tetrahydro-4H-pyrrolo[3,2,1-ij]quinolin-4-one,

or a salt thereof,

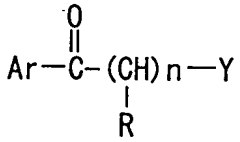
(10) An agent as described in the above item (1) which is a prophylactic and therapeutic agent for dysuria;

(11) An agent as described in the above item (1) which is a prophylactic and therapeutic agent for difficulty of urination; and

(12) Agents for improving excretory potency of the urinary bladder which comprises a combination of an α-blocker and an amine compound of non-carbamate-type having an acetylcholin- esterase-inhibiting action.

The "amine compounds of non-carbamate-type having an acetylcholinesterase-inhibiting action" used in the invention include those which have an acetylcholinesterase-inhibiting action but have no carbamate structure -OCON- in the molecule, and in which the hydrogen atom on ammonia is replaced by a hydrocarbon group, preferably including primary amine compounds, secondary amine compounds, and tertiary amine compounds. More preferably, the following compounds are exemplified. Among these compounds, those which contain at least one 5- to 7-membered nitrogen-containing heterocycle as a partial structure are preferred, and in particular, compounds as described in the following items, 1), 20), 23), 41), 42) and 43) are especially preferred. Among them, particularly preferred are compounds as described in the item 1).

1) Compounds of the formula:



wherein Ar is optionally condensed phenyl which may have a substituent or substituents;

n is an integer of 1 to 10;

R is hydrogen or optionally substituted hydrocarbon group;

Y is optionally substituted amino or optionally substituted nitrogen-containing saturated heterocyclic group;

or salts thereof (hereinafter also abbreviated to as Compound (I)).

In the above-mentioned formula, the "substituent" in "optionally condensed phenyl in which the phenyl moiety may be substituted by a substituent or substituents" represented by Ar includes, for example, (i) optionally halogenated lower alkyl, (ii) halogen (e.g., fluoro, chloro, bromo, iodo, etc.), (iii) lower alkylenedioxy (e.g., C_{1-3} alkylenedioxy such as methylenedioxy, ethylenedioxy, etc.), (iv) nitro, (v) cyano, (vi) hydroxy, (vii) optionally halogenated lower alkoxy, (viii) cycloalkyl (e.g., C_{3-6} cycloalkyl such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, etc.), (ix) optionally halogenated lower alkylthio, (x) amino, (xi) mono-lower alkylamino (e.g.,

mono-C_{1-6} alkylamino such as methylamino, ethylamino, propylamino, etc.), (xii) di-lower alkylamino (e.g., di-C_{1-6} alkylamino such as dimethylamino, diethylamino, etc.), (xiii) 5- to 7-membered cyclic amino (e.g., 5- to 7-membered cyclic amino which may contain 1 to 3 heteroatoms selected from nitrogen, oxygen and sulfur, etc., in addition to one nitrogen atom (e.g., pyrrolidino, piperidino, piperazino, morpholino, thiomorpholino, etc.)), (xiv) lower alkyl-carbonylamino (e.g., C_{1-6} alkyl-carbonylamino such as acetylamino, propionylamino, butyrylamino, etc.), (xv) lower alkyl-sulfonylamino (e.g., C_{1-6} alkylsulfonylamino such as methylsulfonylamino, ethylsulfonylamino, propylsulfonylamino, etc.), (xvi) lower alkoxycarbonyl (e.g., C_{1-6} alkoxy-carbonyl such as methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, isobutoxycarbonyl, etc.), (xvii) carboxy, (xviii) lower alkylcarbonyl (e.g., C_{1-6} alkylcarbonyl such as methylcarbonyl, ethylcarbonyl, butylcarbonyl, etc.), (xix) cycloalkylcarbonyl (e.g., C_{3-6} cycloalkylcarbonyl such as cyclopropylcarbonyl, cyclobutylcarbonyl, cyclopentylcarbonyl, cyclohexylcarbonyl, etc.), (xx) carbamoyl, thiocarbamoyl, (xxi) mono-lower alkyl-carbamoyl (e.g., mono-C_{1-6} alkyl-carbamoyl such as methylcarbamoyl, ethylcarbamoyl, propylcarbamoyl, butylcarbamoyl, etc.), (xxii) di-lower alkyl-carbamoyl (e.g., di-C_{1-6} alkyl-

carbamoyl such as diethylcarbamoyl, dibutylcarbamoyl, etc.), (xxiii) lower alkylsulfonyl (e.g., C_{1-6} alkylsulfonyl such as methylsulfonyl, ethylsulfonyl, propylsulfonyl, etc.), (xxiv) cycloalkylsulfonyl (e.g., C_{3-6} cycloalkylsulfonyl such as cyclopentylsulfonyl, cyclohexylsulfonyl, etc.), (xxv) phenyl, (xxvi) naphthyl, (xxvii) mono-phenyl-lower alkyl (e.g., mono-phenyl-C_{1-6} alkyl such as benzyl, phenylethyl, etc.), (xxviii) di-phenyl-lower alkyl (e.g., di-phenyl-C_{1-6} alkyl such as diphenylmethyl, diphenylethyl, etc.), (xxix) mono-phenyl-lower alkyl-carbonyloxy (e.g., mono-phenyl-C_{1-6} alkyl-carbonyloxy such as phenyl-methylcarbonyloxy, phenylethylcarbonyloxy, etc.), (xxx) di-phenyl-lower alkyl-carbonyloxy (e.g., diphenyl-C_{1-6} alkyl-carbonyloxy such as diphenylmethylcarbonyloxy, diphenylethylcarbonyloxy, etc.), (xxxi) phenoxy, (xxxii) mono-phenyl-lower alkyl-carbonyl (e.g., mono-phenyl-C_{1-6} alkyl-carbonyl such as phenylmethylcarbonyl, phenyl-ethylcarbonyl, etc.), (xxxiii) di-phenyl-lower alkyl-carbonyl (e.g., di-phenyl-C_{1-6} alkyl-carbonyl such as diphenylmethylcarbonyl, diphenylethylcarbonyl, etc.), (xxxiv) benzoyl, (xxxv) phenoxycarbonyl, (xxxvi) phenyl-lower alkyl-carbamoyl (e.g., phenyl-C_{1-6} alkyl-carbamoyl such as phenyl-methylcarbamoyl, phenyl-ethylcarbamoyl, etc.), (xxxvii) phenylcarbamoyl, (xxxviii) phenyl-lower alkyl-carbonylamino (e.g., phenyl-C_{1-6} alkyl-carbonylamino

such as phenyl-methylcarbonylamino, phenyl-ethylcarbonylamino, etc.), (xxxix) phenyl-lower alkylamino (e.g., phenyl-C_{1-6} alkylamino such as phenyl-methylamino, phenyl-ethylamino, etc.), (xxxx) phenyl-lower alkylsulfonyl (e.g., phenyl-C_{1-6} alkylsulfonyl such as phenyl-methyl-sulfonyl, phenyl-ethylsulfonyl, etc.), (xxxxi) phenylsulfonyl, (xxxxii) phenyl-lower alkylsulfinyl (e.g., phenyl-C_{1-6} alkylsulfinyl such as phenyl-methylsulfinyl, phenyl-ethylsulfinyl, etc.), (xxxxiii) phenyl-lower alkylsulfonylamino (e.g., phenyl-C_{1-6} alkylsulfonylamino such as phenyl-methylsulfonylamino, phenyl-ethylsulfonylamino, etc.), and (xxxxiv) phenylsulfonylamino (wherein the phenyl, naphthyl, mono-phenyl-lower alkyl, di-phenyl-lower alkyl, mono-phenyl-lower alkyl-carbonyloxy, di-phenyl-lower alkyl-carbonyloxy, phenoxy, mono-phenyl-lower alkyl-carbonyl, di-phenyl-lower alkyl-carbonyl, benzoyl, phenoxycarbonyl, phenyl-lower alkyl-carbamoyl, phenylcarbamoyl, phenyl-lower alkyl-carbonylamino, phenyl-lower alkylamino, phenyl-lower alkylsulfonyl, phenylsulfonyl, phenyl-lower alkylsulfinyl, phenyl-lower alkylsulfonylamino and phenylsulfonylamino as mentioned above in (xxv) to (xxxxiv) may further be substituted by 1 to 4 substituents selected from lower alkyl (e.g., C_{1-6} alkyl such as methyl, ethyl, propyl, isopropyl, butyl, sec-butyl, tert-butyl, pentyl, hexyl, etc.), lower alkoxy (e.g.,

C_{1-6} alkoxy such as methoxy, ethoxy, propoxy, isopropoxy, butoxy, isobutoxy, sec-butoxy, tert-butoxy, etc.), halogen (e.g., chloro, bromo, iodo, etc.), hydroxy, benzyloxy, amino, mono-lower alkylamino (e.g., mono-C_{1-6} alkylamino such as methylamino, ethylamino, propylamino, etc.), di-lower alkylamino (e.g., di-C_{1-6} alkylamino such as dimethylamino, diethylamino, etc.), nitro, lower alkyl-carbonyl (e.g., C_{1-6} alkyl-carbonyl such as methylcarbonyl, ethylcarbonyl, butylcarbonyl, etc.), benzoyl, and the like). Said phenyl may be substituted by 1 to 4 of these substituents.

The "optionally halogenated lower alkyl " as mentioned above includes, for example, lower alkyl (e.g., C_{1-6} alkyl such as methyl, ethyl, propyl, isopropyl, butyl, sec-butyl, tert-butyl, pentyl, hexyl, etc.) which may have 1 to 3 halogen atoms (e.g. chloro, bromo, iodo, etc.), and is exemplified by methyl, chloromethyl, difluoromethyl, trichloromethyl, trifluoromethyl, ethyl, 2-bromoethyl, 2,2,2-trifluoroethyl, propyl, 3,3,3-trifluoropropyl, isopropyl, butyl, 4,4,4-trifluorobutyl, isobutyl, sec-butyl, tert-butyl, pentyl, isopentyl, neopentyl, 5,5,5-trifluoropentyl, hexyl, 6,6,6-trifluorohexyl, and the like.

The "optionally halogenated lower alkoxy " as mentioned above includes, for example, lower alkoxy (e.g., C_{1-6} alkoxy such as methoxy, ethoxy, propoxy, isopropoxy,

butoxy, isobutoxy, sec-butoxy, tert-butoxy, etc.) which may have 1 to 3 halogen atoms (e.g. chloro, bromo, iodo, etc.), and is exemplified by methoxy, difluoromethoxy, trifluoromethoxy, ethoxy, 2,2,2-trifluoroethoxy, propoxy, isopropoxy, butoxy, 4,4,4-trifluorobutoxy, isobutoxy, sec-butoxy, pentyloxy, hexyloxy, and the like.

The "optionally halogenated lower alkylthio " as mentioned above includes, for example, lower alkylthio (e.g., C_{1-6} alkylthio such as methylthio, ethylthio, propylthio, isopropylthio, butylthio, isobutylthio, sec-butylthio, tert-butylthio, etc.) which may have 1 to 3 halogen atoms (e.g. chloro, bromo, iodo, etc.), and is exemplified by methylthio, difluoromethylthio, trifluoromethylthio, ethylthio, propylthio, isopropylthio, butylthio, 4,4,4-trifluorobutylthio, isobutylthio, sec-butylthio, tert-butylthio, pentylthio, hexylthio, and the like.

The "substituent" in "optionally condensed phenyl which may have a substituent or substituents" includes preferably, (i) amino, (ii) mono-lower alkylamino (e.g., mono-C_{1-6} alkylamino such as methylamino, ethylamino, propylamino, etc.), (iii) di-lower alkylamino (e.g., di-C_{1-6} alkylamino such as dimethylamino, diethylamino, etc.), (iv) 5- to 7-membered cyclic amino which may contain, for example, 1 to 3 heteroatoms selected from nitrogen, oxygen

and sulfur, etc., in addition to one nitrogen atom (e.g., pyrrolidino, piperidino, piperazino, morpholino, thiomorpholino, etc.), (v) lower alkyl-carbonylamino (e.g., C_{1-6} alkyl-carbonylamino such as acetylamino, propionylamino, butyrylamino, etc.), (vi) lower alkyl-sulfonylamino (e.g., C_{1-6} alkylsulfonylamino such as methylsulfonylamino, ethylsulfonylamino, propylsulfonylamino etc.), (vii) phenyl-lower alkylamino (e.g., phenyl-C_{1-6} alkylamino such as phenyl-methylamino, phenyl-ethylamino, etc.), (viii) phenyl-lower alkylsulfonylamino (e.g., phenyl-lower C_{1-6} alkylsulfonylamino such as phenyl-methylsulfonylamino, phenyl-ethylsulfonylamino, etc.), (ix) phenylsulfonylamino, (x) halogen (e.g. fluoro, chloro, etc.), (xi) optionally halogenated lower alkyl (e.g., methyl, ethyl, isopropyl, tert-butyl, trifluoromethyl, etc.) and (xii) optionally halogenated lower alkoxy (e.g., methoxy, ethoxy, isopropoxy, tert-butoxy, trifluoromethoxy, etc.). Particularly preferred are di-lower alkylamino (e.g., di-C_{1-6} alkylamino such as dimethylamino, di-ethylamino, etc.), 5- to 7-membered cyclic amino which may contain 1 to 3 heteroatoms selected from nitrogen, oxygen and sulfur, etc., in addition to one nitrogen atom (e.g., pyrrolidino, piperidino, piperazino, morpholino, thiomorpholino, etc.), and the like.

The condensed "phenyl" of "optionally condensed

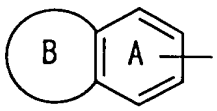
phenyl which may have a substituent or substituents" is exemplified by, for example,

(1) an example in which the phenyl is condensed with an optionally substituted mono-cyclic heterocycle;

(2) an example in which the phenyl is condensed with an optionally substituted bicyclic heterocycle or with two same or different mono-cyclic group (provided that at least one of two is a mono-cyclic heterocycle); and

(3) an example in which the phenyl is condensed with an optionally substituted tricyclic heterocycle.

When the phenyl of "optionally condensed phenyl which may be substituted by a substituent or substituents" is condensed with a mono-cyclic heterocycle, a group of the formula:



wherein the ring A is an optionally substituted benzene ring; and the ring B is an optionally substituted heterocycle;

is exemplified.

As for the substituent on the ring A, the "substituent" of "optionally condensed phenyl which may be substituted by a substituent or substituents" are exemplified. The number of the substituent is 1 to 3.

The "heterocycle" of "optionally substituted

heterocycle" represented by the ring B includes 4- to 14-membered (preferably 5- to 9-membered) aromatic or non-aromatic heterocycles which contain 1 to 4 heteroatoms selected from, for example, nitrogen, oxygen and sulfur. Such heterocycles are exemplified by pyridine, pyrazine, pyrimidine, imidazole, furan, thiophene, dihydropyridine, diazepine, oxazepine, pyrrolidine, piperidine, hexamethylenimine, heptamethylenimine, tetrahydrofuran, piperazine, homopiperazine, tetrahydrooxazepine, morpholine, thiomorpholine, pyrrole, pyrazole, 1,2,3-triazole, oxazole, oxazolidine, thiazole, thiazolidine, isoxazole, imidazoline, and the like. Among these heterocylces, 5- to 9-membered non-aromatic heterocycles containing 1 heteroatom or 2 identical or different heteroatoms (e.g., pyrrolidine, piperidine, hexamethylenimine, heptamethylenimine, tetrahydrofuran, piperazine, homopiperazine, tetrahydrooxazepine, morpholine, thiomorpholine, etc.) are preferred. Particularly preferred are (1) non-aromatic heterocycles containing 1 heteroatom selected from, for example, nitrogen, oxygen and sulfur, and (2) non-aromatic heterocycles containing 1 nitrogen atom and 1 heteroatom selected from nitrogen, oxygen and sulfur.

As the "substituent" of "optionally substituted heterocycle" represented by the ring B, the following 1 to 5 substituents may be used: (i) halogen (e.g., fluoro,

chloro, bromo, iodo, etc.), (ii) nitro, (iii) cyano, (iv) oxo, (v) hydroxy, (vi) lower alkyl (e.g., C_{1-6} alkyl such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, tert-butyl, sec-butyl, etc.), (vii) lower alkoxy (e.g., C_{1-6} alkoxy such as methoxy, ethoxy, propyloxy, isopropyloxy, butyloxy, etc.), (viii) lower alkylthio (e.g., C_{1-6} alkylthio such as methylthio, ethylthio, propylthio, etc.), (ix) amino, (x) mono-lower alkylamino (e.g., mono-C_{1-6} alkylamino such as methylamino, ethylamino, propylamino, etc.), (xi) di-lower alkylamino (e.g., di-C_{1-6} alkylamino such as dimethylamino, diethylamino, etc.), (xii) 5- to 7-membered cyclic amino which may contain 1 to 3 heteroatoms selected from, for example, nitrogen, oxygen and sulfur, in addition to carbon atoms and one nitrogen atom (e.g., pyrrolidino, piperidino, piperazino, morpholino, thiomorpholino, etc.), (xiii) lower alkyl-carbonylamino (e.g., C_{1-6} alkyl-carbonylamino such as acetylamino, propionylamino, butyrylamino, etc.), (xiv) lower alkylsulfonylamino (e.g., C_{1-6} alkylsulfonylamino such as methylsulfonylamino, ethylsulfonylamino, etc.), (xv) lower alkoxy-carbonyl (e.g., C_{1-6} alkoxy-carbonyl such as methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, etc.), (xvi) carboxy, (xvii) lower alkylcarbonyl (e.g., C_{1-6} alkylcarbonyl such as methylcarbonyl, ethylcarbonyl, propylcarbonyl, etc.), (xviii) carbamoyl, (xix) mono-lower

alkylcarbamoyl (e.g., mono-C_{1-6} alkyl-carbamoyl such as methylcarbamoyl, ethylcarbamoyl, etc.), (xx) di-lower alkylcarbamoyl (e.g., di-C_{1-6} alkyl-carbamoyl such as dimethylcarbamoyl, diethylcarbamoyl, etc.), (xxi) lower alkylsulfonyl (e.g., C_{1-6} alkylsulfonyl such as methylsulfonyl, ethylsulfonyl, propylsulfonyl, etc.), and the like. Among these substituents, oxo, lower alkyl (e.g., C_{1-6} alkyl such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, tert-butyl, sec-butyl, etc.), and the like are preferred. Particularly preferred is oxo.

When the ring B contains a nitrogen atom in the ring, it may have a group of the formula:

$$>N-R^1$$

wherein R^1 is hydrogen, optionally substituted hydrocarbon group, acyl, or optionally substituted heterocyclic group; in the ring. In addition, the ring B may contain 1 to 3 of the above-mentioned substituents (i) to (xxi).

The "hydrocarbon group" of "optionally substituted hydrocarbon group" indicates a group which is formed from a hydrocarbon compound by removing one hydrogen atom, and is exemplified, for example, by the following alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, a combination of these groups, and the like. Among these groups, C_{1-16} hydro-carbon group is preferred.

(1) Alkyl (e.g., C_{1-6} alkyl such as methyl, ethyl,

propyl, isopropyl, butyl, isobutyl, tert-butyl, sec-butyl, pentyl, hexyl, etc.)

(2) Alkenyl (e.g., C_{2-6} alkenyl such as vinyl, allyl, isopropenyl, butenyl, isobutenyl, sec-butenyl, etc.)

(3) Alkynyl (e.g., C_{2-6} alkynyl such as propargyl, ethynyl, butynyl, 1-hexynyl, etc.)

(4) Cycloalkyl (e.g., C_{3-6} cycloalkyl such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, etc.)

(5) Crosslinked cyclic lower saturated hydrocarbon group (e.g., Crosslinked cyclic C_{8-14} saturated hydrocarbon group such as bicyclo[3.2.1]oct-2-yl, bicyclo[3.3.1]non-2-yl, adamantan-1-yl, etc.)

(6) Aryl (e.g., C_{6-14} aryl such as phenyl, 1-naphthyl, 2-naphthyl, biphenyl, 2-indenyl, 2-anthryl, etc. Phenyl is preferred.)

(7) Aralkyl (e.g., C_{7-16} aralkyl such as: phenyl-C_{1-10} alkyl such as benzyl, phenylethyl, phenylpropyl, phenylbutyl, phenylpentyl, phenylhexyl, etc.; naphthyl-C_{1-6} alkyl such as α-naphthylmethyl, etc.; diphenyl-C_{1-3} alkyl such as diphenylmethyl, diphenylethyl, etc.)

(8) Aryl-alkenyl (e.g., C_{6-14} aryl-C_{2-12} alkenyl such as: phenyl-C_{2-12} alkenyl such as styryl, cinnamyl, 4-phenyl-2-butenyl, 4-phenyl-3-butenyl, etc.)

(9) Aryl-C_{2-12} alkynyl (e.g., C_{6-14} aryl-C_{2-12} alkynyl such as: phenyl-C_{2-12} alkynyl such as phenylethynyl, 3-

phenyl-2-propynyl, 3-phenyl-1-propynyl, etc.)

(10) Cycloalkyl-alkyl (e.g., C_{3-7} cycloalkyl-C_{1-6} alkyl such as cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl, cyclohexylmethyl, cycloheptylmethyl, cyclopropylethyl, cyclobutylethyl, cyclopentylethyl, cyclohexylethyl, cycloheptylethyl, cyclopropylpropyl, cyclobutylpropyl, cyclopentylpropyl, cyclohexylpropyl, cycloheptylpropyl, cyclopropylbutyl, cyclobutylbutyl, cyclopentylbutyl, cyclohexylbutyl, cycloheptylbutyl, cyclopropylpentyl, cyclobutylpentyl, cyclopentylpentyl, cyclohexylpentyl, cycloheptylpentyl, cyclopropylhexyl, cyclobutylhexyl, cyclopentylhexyl, cyclohexylhexyl, etc.)

(11) Aryl-aryl-C_{1-10} alkyl (e.g., biphenylmethyl, biphenylethyl, etc.)

The "hydrocarbon group" of "optionally substituted hydrocarbon group" represented by R^1 preferably includes, for example, C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{7-16} aralkyl, and the like. Particularly preferred are C_{7-10} aralkyl (e.g., phenyl-C_{1-4} alkyl such as benzyl, phenylethyl, phenylpropyl, etc.), and the like.

As the "substituent" of "optionally substituted hydrocarbon group" represented by R^1, the following 1 to 5 substituents (preferably, 1 to 3 substituents) may be used: (i) halogen (e.g., fluoro, chloro, bromo, iodo, etc.), (ii) nitro, (iii) cyano, (iv) oxo, (v) hydroxy, (vi) optionally

halogenated lower alkyl, (vii) optionally halogenated lower alkoxy, (viii) optionally halogenated lower alkylthio, (ix) amino, (x) mono-lower alkylamino (e.g., mono-C_{1-6} alkylamino such as methylamino, ethylamino, propylamino, etc.), (xi) di-lower alkylamino (e.g., di-C_{1-6} alkylamino such as dimethylamino, diethylamino, etc.), (xii) 5- to 7-membered cyclic amino which may contain 1 to 3 heteroatoms selected from, for example, nitrogen, oxygen and sulfur, etc., in addition to carbon atoms and one nitrogen atom (e.g., pyrrolidino, piperidino, piperazino, morpholino, thiomorpholino, etc.), (xiii) lower alkyl-carbonylamino (e.g., C_{1-6} alkyl-carbonylamino such as acetylamino, propionylamino, butyrylamino, etc.), (xiv) lower alkyl-sulfonylamino (e.g., C_{1-6} alkyl-sulfonylamino such as methylsulfonylamino, ethylsulfonylamino, etc.), (xv) lower alkoxy-carbonyl (e.g., C_{1-6} alkoxy-carbonyl such as methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, etc.), (xvi) carboxy, (xvii) lower alkyl-carbonyl (e.g., C_{1-6} alkyl-carbonyl such as methylcarbonyl, ethylcarbonyl, propylcarbonyl, etc.), (xviii) carbamoyl, thiocarbamoyl, (xix) mono-lower alkyl-carbamoyl (e.g., mono-C_{1-6} alkyl-carbamoyl such as methylcarbamoyl, ethylcarbamoyl, etc.), (xx) di-lower alkyl-carbamoyl (e.g., di-C_{1-6} alkyl-carbamoyl such as dimethylcarbamoyl, diethylcarbamoyl, etc.), (xxi) lower alkylsulfonyl (e.g., C_{1-6} alkylsulfonyl such as methylsulfonyl, ethylsulfonyl,

propylsulfonyl, etc.), (xxii) lower alkoxy-carbonyl-lower alkyl (e.g., C_{1-6} alkyl-carbonyl-C_{1-6} alkyl such as methoxycarbonylmethyl, ethoxycarbonylmethyl, tert-butoxycarbonylmethyl, methoxycarbonylethyl, methoxycarbonylmethyl, methoxycarbonyl(dimethyl)methyl, ethoxycarbonyl(dimethyl)methyl, tert-butoxycarbonyl(dimethyl)methyl, etc.), (xxiii) carboxy-lower alkyl (e.g., carboxy-C_{1-6} alkyl such as carboxylmethyl, carboxylethyl, carboxyl(dimethyl)methyl, etc.), (xxiv) optionally substituted heterocycle, (xxv) C_{6-14} aryl (e.g., phenyl, naphthyl, etc.), (xxvi) C_{7-16} aralkyl (e.g., benzyl, etc.), (xxvii) optionally substituted ureido (e.g., ureido, 3-methylureido, 3-ethylureido, 3-phenylureido, 3-(4-fluorophenyl)ureido, 3-(2-methylphenyl)ureido, 3-(4-methoxyphenyl)ureido, 3-(2,4-difluorophenyl)ureido, 3-[3,5-bis(trifluoromethyl)phenyl]ureido, 3-benzylureido, 3-(1-naphthyl)ureido, 3-(2-biphenylyl)ureido, etc.), (xxviii) optionally substituted thioureido (e.g., thioureido, 3-methylthioureido, 3-ethylthioureido, 3-phenylthioureido, 3-(4-fluorophenyl)thioureido, 3-(4-methylphenyl)thioureido, 3-(4-methoxyphenyl)thioureido, 3-(2,4-dichlorophenyl)thioureido, 3-benzylthioureido, 3-(1-naphthyl)thioureido, etc.), (xxix) optionally substituted amidino (e.g., amidino, N^1-methylamidino, N^1-ethylamidino, N^1-phenylamidino, N^1,N^1-dimethylamidino, N^1,N^2-

dimethylamidino, N^1-methyl-N^1-ethylamidino, N^1,N^1-diethylamidino, N^1-methyl-N^1-phenylamidino, N^1,N^1-di(4-nitrophenyl)amidino, etc.), (xxx) optionally substituted guanidino (e.g., guanidino, 3-methylguanidino, 3,3-dimethylguanidino, 3,3-diethylguanidino, etc.), (xxxi) optionally substituted cyclic aminocarbonyl (e.g., pyrrolidinocarbonyl, piperidinocarbonyl, (4-methylpiperidino)carbonyl, (4-phenylpiperidino)carbonyl, (4-benzylpiperidino)carbonyl, (4-benzoylpiperidino)carbonyl, [4-(4-fluorobenzoyl)piperidino]carbonyl, (4-methylpiperazino)carbonyl, (4-phenylpiperazino)carbonyl, [4-(4-nitrophenyl)piperazino]-carbonyl, (4-benzylpiperazino)carbonyl, morpholinocarbonyl, thiomorpholinocarbonyl, etc.), (xxxii) optionally substituted aminothiocarbonyl (e.g., aminothiocarbonyl, methylaminothiocarbonyl, dimethylaminothiocarbonyl, etc.), (xxxiii) optionally substituted aminosulfonyl (e.g., aminosulfonyl, methylaminosulfonyl, dimethylaminosulfonyl, etc.), (xxxiv) optionally substituted phenylsulfonylamino (e.g., phenylsulfonylamino, (4-methylphenyl)sulfonylamino, (4-chlorophenyl)sulfonylamino, (2,5-dichlorophenyl)sulfonylamino, (4-methoxyphenyl)sulfonylamino, (4-acetylamino-phenyl)sulfonylamino, (4-nitrophenyl)phenylsulfonylamino, etc.), (xxxv) sulfo, (xxxvi) sulfino, (xxxvii) sulfeno,

(xxxviii) C_{1-6} alkylsulfo (e.g., methylsulfo, ethylsulfo, propylsulfo, etc.), (xxxix) C_{1-6} alkylsulfino (e.g., methylsulfino, ethylsulfino, propylsulfino, etc.), (xxxx) C_{1-6} alkylsulfeno (e.g., methylsulfeno, ethylsulfeno, propylsulfeno, etc.), (xxxxi) phosphono, (xxxxii) di-C_{1-6} alkoxyphosphoryl (e.g., dimethoxyphosphoryl, diethoxyphosphoryl, dipropoxyphosphoryl, etc.).

Among these substituents, preferred ones include halogen, optionally halogenated alkyl, optionally halogenated alkoxy, hydroxy, nitro, cyano, carboxy, C_{1-6} alkoxy-carbonyl, carbamoyl, aminothiocarbonyl, mono-C_{1-6} alkyl-carbamoyl, di-C_{1-6} alkyl-carbamoyl, amino, mono-C_{1-6} alkylamino, di-C_{1-6} alkylamino, 5- to 7-membered cyclic amino, C_{1-6} alkyl-carbonylamino, phenylsulfonylamino, C_{1-6} alkylsulfonylamino, and the like.

As the "heterocyclic group" of "optionally substituted heterocyclic group" above-mentioned, for example, a group may be used which is formed from a 5- to 14-membered (monocyclic or bi- to tetra-cyclic) heterocycle containing 1 to 6 (preferably, 1 to 4) heteroatoms selected from nitrogen, oxygen, sulfur and the like by removing one hydrogen atom.

The monocyclic heterocyclic group includes those derived from the following monocyclic heterocycles by removing one hydrogen atom: pyridine, pyrazine, pyrimidine,

imidazole, furan, thiophene, dihydropyridine, diazepine, oxazepine, pyrrolidine, piperidine, hexamethylenimine, heptamethylenimine, tetrahydrofuran, piperazine, homopiperazine, tetrahydrooxazepine, morpholine, thiomorpholine, pyrrole, pyrazole, 1,2,3-triazole, oxazole, oxazolidine, thiazole, thiazolidine, isoxazole, imidazoline, triazole, thiadiazole, oxadiazole, oxathiadiazole, triazine, tetrazole, and the like.

The bicyclic heterocyclic group includes those derived from the following bicyclic heterocycles by removing one hydrogen atom: indole, dihydroindole, isoindole, dihydroisoindole, benzofuran, dihydrobenzofuran, benzimidazole, benzoxazole, benzisoxazole, benzothiazole, indazole, quinoline, tetrahydroquinoline, isoquinoline, tetrahydroisoquinoline, tetrahydro-1H-1-benzazepine, tetrahydro-1H-2-benzazepine, tetrahydro-1H-3-benzazepine, tetrahydrobenzoxazepine, quinazoline, tetrahydroquinazoline, quinoxaline, tetrahydroquinoxaline, benzodioxane, benzodioxole, benzothiazine, imidazopyridine, and the like.

The tri- or tetra-cyclic heterocyclic group includes those derived from the following tri- or tetra-cyclic heterocycles by removing one hydrogen atom: acridine, tetrahydroacridine, pyrroloquinoline, pyrroloindole, cyclopentaindole, isoindolobenzazepine, and the like.

The "heterocyclic group" preferably includes

those derived from monocyclic or bicyclic heterocycles by removing one hydrogen atom.

As for the "substituent" in said "optionally substituted heterocyclic group", those of "optionally substituted heterocycles" represented by the above-mentioned ring B are exemplified. The number of the substituents is 1 to 5.

The "optionally substituted hydrocarbon group" represented by R^1 preferably includes C_{7-16} aralkyl (preferably, benzyl, etc.) which may contain 1 to 5 of substituents selected from halogen, C_{1-6} alkyl, C_{1-6} alkoxy, nitro, cyano and hydroxy.

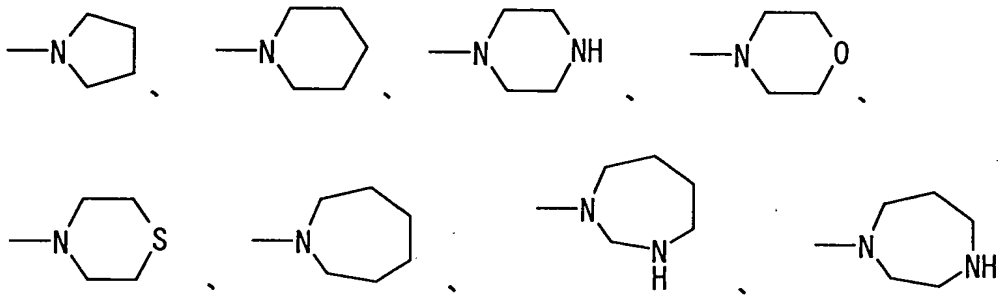
The "acyl" represented by the above-mentioned R^1 includes those indicated by the formula: $-(C=O)-R^2$, $-(C=O)-OR^2$, $-(C=O)-NR^2R^3$, $-SO_2-R^2$, $-SO-R^2$, $-(C=S)-OR^2$ or $-(C=S)NR^2R^3$ [wherein R^2 and R^3 each is (i) hydrogen atom, (ii) optionally substituted hydrocarbon group or (iii) optionally substituted heterocyclic group, or R^2 and R^3 taken each other together with the adjacent nitrogen atom may form an optionally substituted nitrogen-containing cyclic group].

Among these groups, the acyl of the formula $-(C=O)-R^2$ or $-(C=O)-NR^2R^3$ [wherein each symbol has the same significance as mentioned above] is preferred.

The "optionally substituted hydrocarbon group"

and "optionally substituted heterocyclic group" represented by R^2 or R^3, respectively include the same groups as the "optionally substituted hydrocarbon group" and "optionally substituted heterocyclic group" represented by the above-mentioned R^1.

The "optionally substituted nitrogen-containing cyclic group" formed by R^2 and R^3 includes 5- to 9-membered (preferably, 5- to 7-membered) nitrogen-containing saturated heterocyclic group which may contain 1 to 3 heteroatoms selected from, for example, nitrogen, oxygen and sulfur, in addition to carbon atoms and one nitrogen atom. Such a group is exemplified, for example, by groups of the formulae:



As for the "substituent" of "optionally substituted nitrogen-containing cyclic group", the same ones as in the "optionally substituted heterocycle" represented by the aforementioned ring B are exemplified. The number of the substituent is 1 to 5.

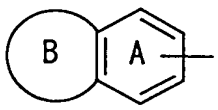
R^2 and R^3 preferably includes (i) hydrogen, (ii) optionally halogenated C_{1-6} alkyl, (iii) C_{6-10} aryl

optionally substituted by 1 to 3 substituents selected from C_{1-6} alkyl and C_{1-6} alkoxy, (iv) C_{7-16} aralkyl (e.g., benzyl, etc.), (v) 5- or 6-membered heterocyclic group (e.g., pyridyl, thienyl, furyl, etc.), and the like.

The "acyl " represented by the above-mentioned R^1, preferably, includes formyl, optionally halogenated C_{1-6} alkyl- carbonyl (e.g., acetyl, trifluoroacetyl, propionyl, etc.), 5- or 6-membered heterocycle-carbonyl (e.g., pyridylcarbonyl, thienylcarbonyl, furylcarbonyl, etc.), C_{6-14} aryl-carbonyl (e.g., benzoyl, 1-naphthoyl, 2-naphthoyl, etc.), C_{7-16} aralkyl-carbonyl (e.g., phenylacetyl, 3-phenylpropionyl, etc.), C_{6-10} aryl-sulfonyl (e.g., benzenesulfonyl, naphthylsulfonyl, etc.), and the like.

R^1 is, preferably, hydrogen, C_{1-6} alkyl, C_{1-6} alkyl-carbonyl, C_{6-14} aryl-carbonyl, and the like.

The group of the above-mentioned formula:



includes groups derived from bicyclic condensed benzene rings by removing one hydrogen atom, which are exemplified by 2,3-dihydrobenzofuran; 3,4-dihydro-2H-1-benzothiopyran; 2,3-dihydro-1H-indole; 1,2,3,4-tetrahydroquinoline; 2,3-dihydro-1H-isoindole; 1,2,3,4-tetrahydroisoquinoline; benzazepine such as 2,3,4,5-tetrahydro-1H-1-benzazepine, 2,3,4,5-tetrahydro-1H-2-benzazepine, 2,3,4,5-tetrahydro-1H-

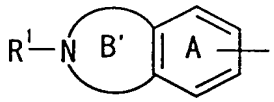
3-benzazepine, etc.; benzazocine such as 1,2,3,4,5,6-hexahydro-1-benzazocine, 1,2,3,4,5,6-hexahydro-2-benzazocine, 1,2,3,4,5,6-hexahydro-3-benzazocine, etc.; benzazonine such as 2,3,4,5,6,7-hexahydro-1H-1-benzazonine, 2,3,4,5,6,7-hexahydro-1H-2-benzazonine, 2,3,4,5,6,7-hexahydro-1H-3-benzazonine, 2,3,4,5,6,7-hexahydro-1H-4-benzazonine, etc.; benzoxazole such as 2,3-dihydrobenzoxazole, etc.; benzothiazole such as 2,3-dihydrobenzothiazole, etc.; benzimidazole such as 2,3-dihydro-1H-benzimidazole, etc.; benzoxazine such as 3,4-dihydro-1H-2,1-benzoxazine, 3,4-dihydro-1H-2,3-benzoxazine, 3,4-dihydro-2H-1,2-benzoxazine, 3,4-dihydro-2H-1,4-benzoxazine, 3,4-dihydro-2H-1,3-benzoxazine, 3,4-dihydro-2H-3,1-benzoxazine, etc.; benzothiazine such as 3,4-dihydro-1H-2,1-benzothiazine, 3,4-dihydro-1H-2,3-benzothiazine, 3,4-dihydro-2H-1,2-benzothiazine, 3,4-dihydro-2H-1,4-benzothiazine, 3,4-dihydro-2H-1,3-benzothiazine, 3,4-dihydro-2H-3,1-benzothiazine, etc.; benzodiazine such as 1,2,3,4-tetrahydrocinnoline, 1,2,3,4-tetrahydrophthalazine, 1,2,3,4-tetrahydroquinazoline, 1,2,3,4-tetrahydroquinoxaline, etc.; benzoxathiin such as 3,4-dihydro-1,2-benzoxathiin, 3,4-dihydro-2,1-benzoxathiin, 2,3-dihydro-1,4-benzoxathiin, 1,4-dihydro-2,3-benzoxathiin, 4H-1,3-benzoxathiin, 4H-3,1-benzoxathiin, etc.; benzodioxin such as 3,4-dihydro-1,2-benzodioxin, 2,3-dihydro-1,4-

benzodioxin, 1,4-dihydro-2,3-benzodioxin, 4H-1,3-benzodioxin, etc.; benzdithiin such as 3,4-dihydro-1,2-benzdithiin, 2,3-dihydro-1,4-benzdithiin, 1,4-dihydro-2,3-benzdithiin, 4H-1,3-benzdithiin, etc.; benzoxazepine such as 2,3,4,5-tetrahydro-1,2-benzoxazepine, 2,3,4,5-tetrahydro-1,3-benzoxazepine, 2,3,4,5-tetrahydro-1,4-benzoxazepine, 2,3,4,5-tetrahydro-1,5-benzoxazepine, 1,3,4,5-tetrahydro-2,1-benzoxazepine, 1,3,4,5-tetrahydro-2,3-benzoxazepine, 1,3,4,5-tetrahydro-2,4-benzoxazepine, 1,2,4,5-tetrahydro-3,1-benzoxazepine, 1,2,4,5-tetrahydro-3,2-benzoxazepine, 1,2,3,5-tetrahydro-4,1-benzoxazepine, etc.; benzothiazepine such as 2,3,4,5-tetrahydro-1,2-benzothiazepine, 2,3,4,5-tetrahydro-1,4-benzothiazepine, 2,3,4,5-tetrahydro-1,5-benzothiazepine, 1,3,4,5-tetrahydro-2,1-benzothiazepine, 1,3,4,5-tetrahydro-2,4-benzothiazepine, 1,2,4,5-tetrahydro-3,1-benzothiazepine, 1,2,4,5-tetrahydro-3,2-benzothiazepine, 1,2,3,5-tetrahydro-4,1-benzothiazepine, etc.; benzodiazepine such as 2,3,4,5-tetrahydro-1H-1,2-benzodiazepine, 2,3,4,5-tetrahydro-1H-1,3-benzodiazepine, 2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, 2,3,4,5-tetrahydro-1H-1,5-benzodiazepine, 2,3,4,5-tetrahydro-1H-2,3-benzodiazepine, 2,3,4,5-tetrahydro-1H-2,4-benzodiazepine, etc.; benzodioxepine such as 4,5-dihydro-1,3-benzodioxepine, 4,5-dihydro-3H-1,2-benzodioxepine, 2,3-dihydro-5H-1,4-benzodioxepine, 3,4-dihydro-1H-1,5-

benzodioxepine, 4,5-dihydro-1H-2,3-benzodioxepine, 1,5-dihydro-2,4-benzodioxepine, etc.; benzothiepine such as 4,5-dihydro-1H-2,3-benzothiepine, 1,5-dihydro-2,4-benzothiepine, 3,4-dihydro-2H-1,5-benzothiepine, 2,3-dihydro-5H-1,4-benzothiepine, etc.; benzoxazocine such as 3,4,5,6-tetrahydro-2H-1,5-benzoxazocine, 3,4,5,6-tetrahydro-2H-1,6-benzoxazocine, etc.; benzothiazocine such as 3,4,5,6-tetrahydro-2H-1,5-benzothiazocine, 3,4,5,6-tetrahydro-2H-1,6-benzothiazocine, etc.; benzodiazocine such as 1,2,3,4,5, 6-hexahydro-1,6-benzodiazocine, etc.; benzoxathiocine such as 2,3,4,5-tetrahydro-1,6-benzoxathiocine, etc.; benzodioxocine such as 2,3,4,5-tetrahydro-1,6-benzodioxocine, etc.; benzotrioxepine such as 1,3,5-benzotrioxepine, 5H-1,3,4-benzotrioxepine, etc.; benzoxathiazepine such as 3,4-dihydro-2H-5,2,1-benzoxathiazepine, 3,4-dihydro-2H-5,1,2-benzoxathiazepine, 4,5-dihydro-3,1,4-benzoxathiazepine, 4,5-dihydro-3H-1,2,5-benzoxathiazepine, etc.; benzoxadiazepine such as 2,3,4,5-tetrahydro-1,3,4-benzoxadiazepine, etc.; benzthiadiazepine such as 2,3,4,5-tetrahydro-1,3,5-benzthiadiazepine, etc.; benzotriazepine such as 2,3,4,5-tetrahydro-1H-1,2,5-benzotriazepine, etc.; 4,5-dihydro-1,3,2-benzoxathiepine, 4,5-dihydro-1H-2,3-benzoxathiepine, 3,4-dihydro-2H-1,5-benzoxathiepine, 4,5-dihydro-3H-1,2-benzoxathiepine, 4,5-dihydro-3H-2,1-benzoxathiepine, 2,3-dihydro-5H-1,4-

benzoxathiepine, 2,3-dihydro-5H-4,1-benzoxathiepine, etc.; particularly, 2,3,4,5-tetrahydro-1H-3-benzazepine, 2,3,4,5-tetrahydro-1H-2-benzazepine, 2,3-dihydro-1H-indole, 2,3,4,5-tetrahydro-1,4-benzoxazepine, and the like.

Among these groups, preferred ones are exemplified by groups of the formula:

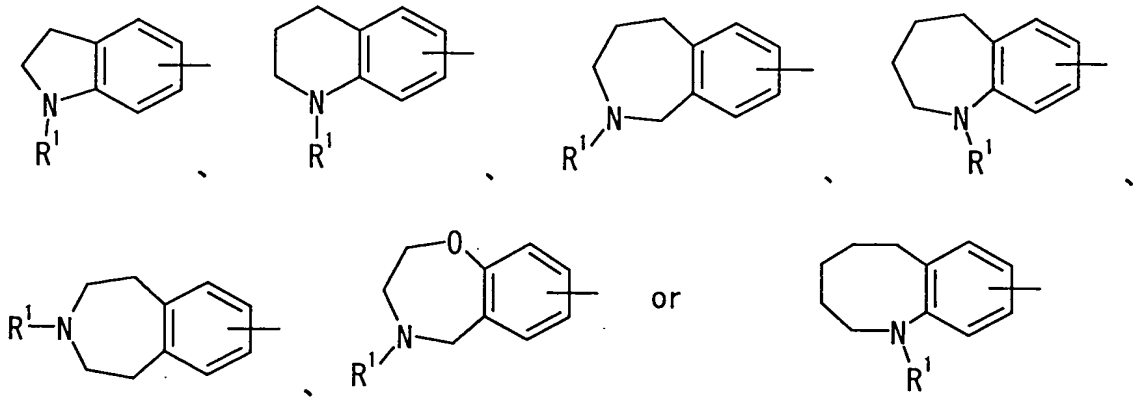


[wherein the ring B' is a 5- to 9-membered nitrogen-containing heterocycle which may further be substituted by oxo; the other symbols have the same significance as mentioned above].

The "5- to 9-membered nitrogen-containing heterocycle" of said "5- to 9-membered nitrogen-containing heterocycle which may further be substituted by oxo" includes 5- to 9-membered nitrogen-containing heterocycles which may contain 1 to 3 heteroatoms selected from, for example, nitrogen, oxygen and sulfur, in addition to carbon atoms and one nitrogen atom. Preferably, 5- to 9-membered non-aromatic nitrogen-containing heterocycles (e.g., pyrrolidine, piperidine, hexamethylenimine, heptamethylenimine, piperazine, homopiperazine, tetrahydrooxazepine, morpholine, thiomorpholine, etc.) may be used.

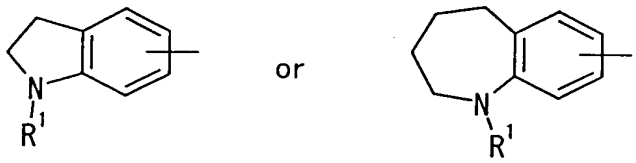
Among these heterocycles, particularly preferred

ones are exemplified by the groups of the formula:



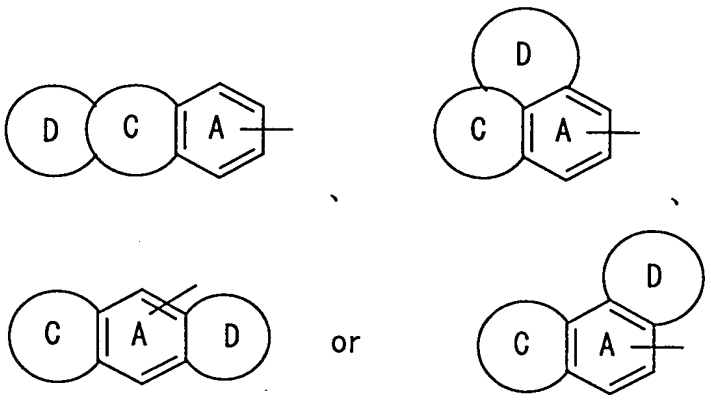
[wherein R^1 has the same significance as mentioned above].

Particularly preferred are the groups represented by the formula:



[wherein R^1 has the same significance as mentioned above].

When the phenyl of "optionally condensed phenyl which may have a substituent or substituents" in the above-mentioned item (2), is condensed with an optionally substituted bicyclic heterocycle or with two identical or different monocycles (provided that at least one of them is a monocyclic heterocycle), such groups are exemplified by those of the formula:



[wherein the ring A has the same significance as mentioned above; one of the rings C and D is an optionally substituted heterocycle and the other is an optionally substituted 5- to 9-membered ring].

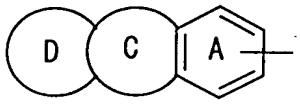
As for the "heterocycle" of "optionally substituted heterocycle" represented by the ring C or D, those of "optionally substituted heterocycle" represented by the ring B are exemplified.

The "5- to 9-membered ring" of "optionally substituted 5- to 9-membered ring" represented by the ring C or D may have 1 to 3 heteroatoms selected from nitrogen, oxygen and sulfur, and includes, for example, 5- to 9-membered heterocycles (e.g., pyridine, pyrazine, pyrimidine, imidazole, furan, thiophene, dihydropyridine, diazepine, oxazepine, pyrrolidine, piperidine, hexamethylenimine, heptamethylenimine, tetrahydrofuran, piperazine, homopiperazine, tetrahydrooxazepine, morpholine, thiomorpholine, etc.), 5- to 9-membered carbocycles (e.g.,

benzene, cyclopentane, cyclopentene, cyclohexane, cyclohexene, cyclohexadiene, cycloheptane, cycloheptene, cycloheptadiene, etc.), and the like. Among them, those of the 5- to 7-membered rings are preferred. Benzene, cyclohexane, and the like are particularly preferred.

As for the "substituent" of "optionally substituted 5- to 9-membered ring", the same "substituent" as in "optionally substituted heterocycle" represented by the above-mentioned ring B may be exemplified.

The group of the above-mentioned formula:

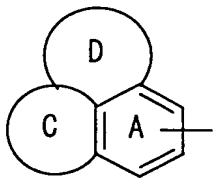


[wherein each symbol has the same significance as mentioned above]

includes the groups derived from tricyclic condensed benzene rings by removing one hydrogen atom, which are exemplified by carbazole, 1,2,3,4,4a,9a-hexahydrocarbazole, 9,10-dihydroacridine, 1,2,3,4-tetrahydroacridine, 10,11-dihydro-5H-dibenz[b,f]azepine, 5,6,7,12-tetraydrodibenz[b,g]azocine, 6,11-dihydro-5H-dibenz[b,e]azepine, 6,7-dihydro-5H-dibenz[c,e]azepine, 5,6,11,12-tetrahydrodibenz[b,f]azocine, dibenzofuran, 9H-xanthene, 10,11-dihydrodibenz[b,f]oxepine, 6,11-dihydrodibenz[b,e]oxepine, 6,7-dihydro-5H-

dibenz[b,g]oxocine, dibenzothiophene, 9H-thioxanthene, 10,11-dihydro-dibenzo[b,f]thiepine, 6,11-dihydrodibenzo[b,e]thiepine, 6,7-dihydro-5H-dibenzo[b,g]thiocine, 10H-phenothiazine, 10H-phenoxazine, 5,10-dihydrophenazine, 10,11-dibenzo[b,f][1,4]thiazepine, 10,11-dihydrodibenz[b,f][1,4]oxazepine, 2,3,5,6,11,11a-hexahydro-1H-pyrrolo[2,1-b][3]benzazepine, 10,11-dihydro-5H-dibenzo[b,e][1,4]diazepine, 5,11-dihydrodibenz[b,e][1,4]oxazepine, 5,11-dihydrodibenzo[b,f][1,4]thiazepine, 10,11-dihydro-5H-dibenzo[b,e][1,4]diazepine, 1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole, and the like.

The group of the above-mentioned formula:

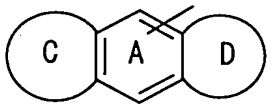


[wherein each symbol has the same significance as mentioned above]

includes the groups derived from tricyclic condensed benzene rings by removing one hydrogen atom, which are exemplified by 1H,3H-naphtho[1,8-cd][1,2]oxazine, naphtho[1,8-de]-1,3-oxazine, naphtho[1,8-de]-1,2-oxazine, 1,2,2a,3,4,5-hexahydrobenz[cd]indole, 2,3,3a,4,5,6-hexahydro-1H-benzo[de]quinoline, 4H-pyrrolo[3,2,1-

ij]quinoline, 1,2,5,6-tetrahydro-4H-pyrrolo[3,2,1-ij]quinoline, 5,6-dihydro-4H-pyrrolo-[3,2,1-ij]quinoline, 1H,5H-benzo[ij]quinolizine, azepino[3,2,1-hj]indole, 1,2,4,5,6,7-hexahydroazepino[3,2,1-hi]indole, 1H-pyrido[3,2,1-jk][1]benzazepine, 5,6,7,8-tetrahydro-1H-pyrido[3,2,1-jk][1]benzazepine, 1,2,5,6,7,8-hexahydro-1H-pyrido[3,2,1-jk][1]benzazepine, 2,3-dihydro-1H-benz[de]isoquinoline, 1,2,3,4,4a,5,6,7-octahydronaphtho-[1,8-bc]azepine, 2,3,5,6,7,8-hexahydro-1H-pyrido[3,2,1-jk][1]benzazepine, and the like.

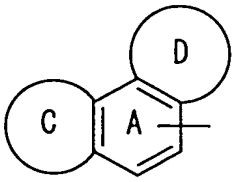
The group of the above-mentioned formula:



[wherein each symbol has the same significance as mentioned above]

includes the groups derived from tricyclic condensed benzene rings by removing one hydrogen atom, which are exemplified by 1,2,3,5,6,7-hexahydrobenzo[1,2-b:4,5-b']dipyrrole, 1,2,3,5,6,7-hexahydrocyclopent[f]indole, and the like.

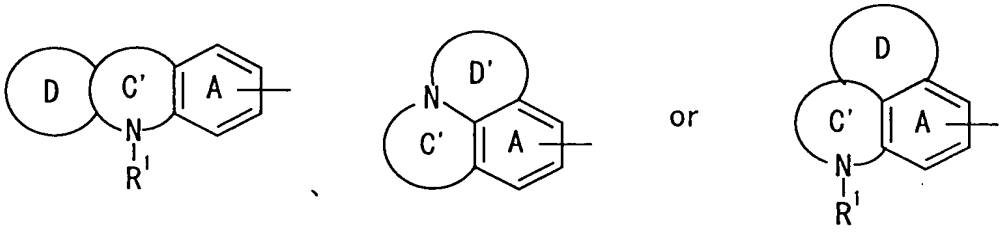
The group of the above-mentioned formula:



[wherein each symbol has the same significance as mentioned above]

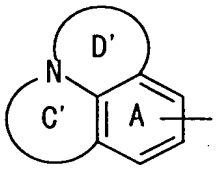
includes the groups derived from tricyclic condensed benzene rings by removing one hydrogen atom, which are exemplified by 1,2,3,6,7,8-hexahydrocyclopent[e]indole, 2,3,4,7,8,9-hexahydro-1H-cyclopenta[f]quinoline, and the like.

Among these groups, preferred ones are exemplified by the groups of the formula:



[wherein the rings C' and D' each is a 5- to 9-membered nitrogen-containing heterocycle which may further be substituted by oxo; the other symbols have the same significance as mentioned above]

Among them, the groups of the formula:

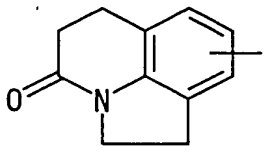


[wherein each symbol has the same significance as mentioned above]

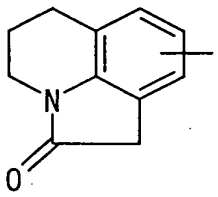
are particularly preferred.

As for the "5- to 9-membered nitrogen-containing heterocycle which may further be substituted by oxo" represented by the ring C' or D', the same as in "5- to 9-membered nitrogen-containing heterocycle which may further be substituted by oxo" represented by the ring B' may be exemplified.

Among them, the group of the formula:

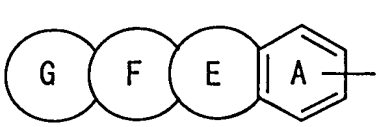


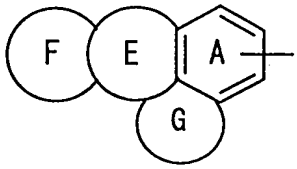
or



is particularly preferred.

When the phenyl group of "optionally condensed phenyl group which may have a substituent or substituents" in the above-mentioned item (3), is condensed with an optionally substituted tricyclic heterocycle, such groups are exemplified by those of the formula:



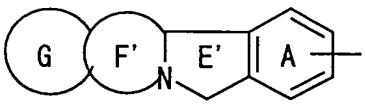
or


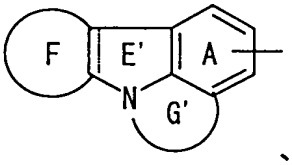
[wherein the ring A has the same significance as mentioned above; at least one of the rings E, F and G is an optionally substituted heterocycle and the other is an optionally substituted 5- to 9-membered ring]

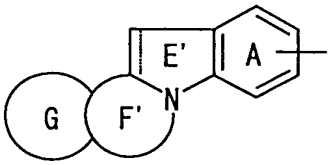
The "optionally substituted heterocycle" and "optionally substituted 5- to 9-membered ring" represented by the ring E, F or G are exemplified by "optionally substituted heterocycle" and "optionally substituted 5- to 9-membered ring" represented by the ring B or C.

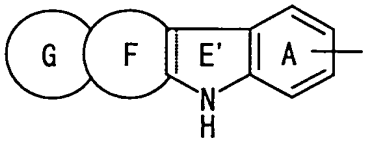
Among them, the followings are preferred:

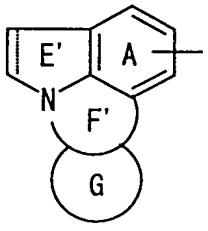
(i) Groups of the formula:









or


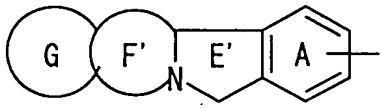
[wherein the ring A has the same significance as mentioned above; the rings E', F' and G' each is a 5- to 9-membered nitrogen-containing heterocycle which may further be

substituted by oxo; and ⎯⎯ indicates a single bond or double bond];

(ii) Groups derived from cyclic compounds by removing one hydrogen atom, which are exemplified by fluoranthene, acephenanthrylene, aceanthrylene, triphenylene, pyrene, chrysene, naphthacene, pleiadene, benzo[a]anthracene, indeno[1,2-a]indene, cyclopenta[a]phenanthrene, pyrido-[1',2':1,2]imidazo[4,5-b]quinoxaline, 1H-2-oxapyrene, spiro[piperidin-4,9'-xanthene], and the like; and their dihydro-, tetrahydro-, hexahydro-, octahydro-, decahydro-derivatives, etc.

As for the "5- to 9-membered nitrogen-containing heterocycle which may further be substituted by oxo" represented by the ring E', F' or G', the same as in "5- to 9-membered nitrogen- containing heterocycle which may further be substituted by oxo" represented by the ring B' may be exemplified.

The group of the above-mentioned formula:



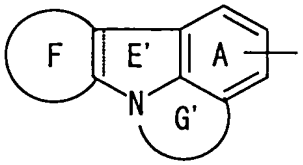
[wherein each symbol has the same significance as mentioned above]

includes the groups derived from tetracyclic condensed benzene rings by removing one hydrogen atom, which are exemplified by 2H-isoindolo[2,1-e]purine, 1H-

pyrazolo[4',3':3,4]pyrido[2,1-a]isoindole, 1H-pyrido[2',3':4,5]imidazo[2,1-a]isoindole, 2H,6H-pyrido[1',2':3,4]imidazo[5,1-a]isoindole, 1H-isoindolo[2,1-a]benzimidazole, 1H-pyrido[3',4':4,5]pyrrolo[2,1-a]isoindole, 2H-pyrido[4',3':4,5]pyrrolo[2,1-a]isoindole, 1H-isoindolo[2,1-a]indole, 2H-isoindolo[1,2-a]isoindole, 1H-cyclopenta[4,5]pyrimido[2,1-a]isoindole, 2H,4H-pyrano[4',3':4,5][1,3]oxazino[2,3-a]isoindole, 2H-isoindolo[2,1-a][3,1]benzoxazine, 7H-isoindolo-[1,2-b][1,3]benzoxazine, 2H-pyrido[2',1':3,4]pyrazino[2,1-a]isoindole, pyrido[2',3':4,5]pyrimido[2,1-a]isoindole, pyrido[3',2':5, 6]pyrimido[2,1-a]isoindole, 1H-pyrido[1',2':3,4]pyrimido[2,1-a]isoindole, isoindolo[2,1-a]quinazoline, isoindolo[2,1-a]quinoxaline, isoindolo[1,2-a]isoquinoline, isoindolo[2,1-b]isoquinoline, isoindolo[2,1-a]quinoline, 6H-oxazino-[3',4':3,4][1,4]diazepino[2,1-a]isoindole, azepino[2',1':3,4]pyrazino[2,1-a]isoindole, 2H,6H-pyrido[2',1':3,4][1,4]-diazepino[2,1-a]isoindole, 1H-isoindolo[1,2-b][1,3,4]benzotriazepine, 2H-isoindolo[2,1-a][1,3,4]benzotriazepine, isoindolo[2,1-d][1,4]benzoxazepine, 1H-isoindolo[2,1-b][2,4]-benzodiazepine, 1H-isoindolo[2,1-c][2,3]benzodiazepine, 2H-isoindolo[1,2-a][2,4]benzodiazepine, 2H-isoindolo[2,1-d]-[1,4]benzodiazepine, 5H-indolo[2,1-b][3]benzazepine, 2H-

isoindolo[1,2-a][2]benzazepine, 2H-isoindolo[1,2-b][3]-benzazepine, 2H-isoindolo[2,1-b][2]benzazepine, 2H-isoindolo[1,2-b][1,3,4]benzoxazocine, isoindolo[2,1-b][1,2,6]benzotriazocine, 5H-4,8-methano-1H-[1,5]diazacycloundecino[1,11-a]indole, and the like.

The group of the above-mentioned formula:

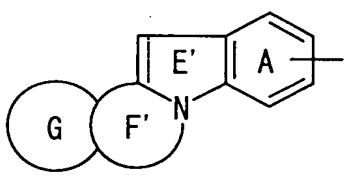


[wherein each symbol has the same significance as mentioned above]

includes the groups derived from tetracyclic condensed benzene rings by removing one hydrogen atom, which are exemplified by 1H,4H-pyrrolo[3',2':4,5]pyrrolo[3,2,1-ij]quinoline, pyrrolo[3,2,1-jk]carbazole, 1H-furo[2',3':4,5]pyrrolo[3,2,1-ij]-quinoline, 1H,4H-cyclopenta[4,5]pyrrolo[1,2,3-de]quinoxaline, 1H,4H-cyclopenta[4,5]pyrrolo[3,2,1-ij]quinoline, pyrido[3',4':4,5]pyrrolo[1,2,3-de]benzoxazine, [1,4]oxazino[2,3,4-jk]carbazole, 1H,3H-[1,3]oxazino[5,4,3-jk]carbazole, pyrido[3',4':4,5]pyrrolo[1,2,3-de][1,4]benzothiazine, 4H-pyrro[3,2,1-de]phenanthridine, 4H,5H-pyrido[3,2,1-de]phenanthridine, 1H,4H-3a,6a-diazafluoroanthene, 1-oxa-4,6a-diazafluoroanthene, 4-oxa-2,10b-diazafluoroanthene, 1-thia-4,6a-diazafluoroanthene,

1H-pyrazino[3,2,1-jk]carbazole, 1H-indolo[3,2,1-de][1,5]naphthyridine, benzo[b]pyrano[2,3,4-hi]indolizine, 1H,3H-benzo[b]pyrano[3,4,5-hi]indolizine, 1H,4H-pyrano[2',3':4,5]pyrrolo[3,2,1-ij]quinoline, 1H,3H-benzo[b]thiopyrano[3,4,5-hi]indolizine, 1H-pyrido[3,2,1-jk]carbazole, 4H-3-oxa-11b-azacyclohepta[jk]fluorene, 2H-azepino[1',2':1,2]pyrimidino[4,5-b]indole, 1H,4H-cyclohepta[4,5]pyrrolo[1,2,3-de]quinoxaline, 5H-pyrido[3',4':4,5]pyrrolo[1,2,3-ef][1,5]benzoxazepine, 4H-pyrido[3',4':4,5]pyrrolo[3,2,1-jk][4,1]benzothiazepine, 5H-pyrido[3',4':4,5]pyrrolo[1,2,3-ef][1,5]benzothiazepine, 5H-pyrido[4',3':4,5]pyrrolo[1,2,3-ef][1,5]benzothiazepine, [1,2,4]triazepino[6,5,4-jk]carbazole, [1,2,4]triazepino[6,7,1-jk]carbazole, [1,2,5]triazepino[3,4,5-jk]carbazole, 5H-[1,4]oxazepino-[2,3,4-jk]carbzole, 5H-[1,4]thiazepino[2,3,4-jk]carbazole, [1,4]diazepino[3,2,1-jk]carbazole, [1,4]diazepino[6,7,1-jk]carbazole, azepino[3,2,1-jk]carbazole, 1H-cycloocta[4,5]pyrrolo[1,2,3-de]quinoxaline, 1H-cycloocta[4,5]pyrrolo[3,2,1-ij]quinoline, and the like.

The group of the above-mentioned formula:



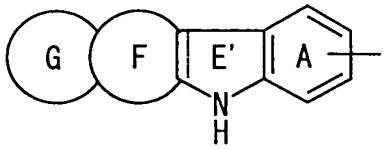
[wherein each symbol has the same significance as mentioned

above]

includes the groups derived from tetracyclic condensed benzene rings by removing one hydrogen atom, which are exemplified by 1H-indolo[1,2-a]benzimidazole, 1H-indolo[1,2-b]indazole, pyrrolo[2',1':3,4]pyrazino[1,2-a]indole, 1H,5H-pyrrolo[1',2':4,5]pyrazino[1,2-a]indole, 2H-pyrido[2',3':3,4]pyrrolo[1,2-a]indole, 1H-pyrrolo[2',3':3,4]pyrido[1,2-a]indole, 1H-indolo[1,2-a]indole, 6H-isoindolo[2,1-a]indole, 6H-indolo[1,2-c][1,3]benzoxazine, 1H-indolo[1,2-b][1,2]benzothiazine, pyrimido[4',5':4,5]pyrimido[1,6-a]indole, pyrazino[2',3':3,4]pyrrido[1,2-a]indole, 6H-pyrido[1',2':3,4]pyrimido[1,6-a]indole, indolo[1,2-b]cinnoline, indolo-[1,2-a]quinazoline, indolo[1,2-c]quinazoline, indolo[2,1-b]quinazoline, indolo[1,2-a]quinoxaline, indolo[1,2-a]-[1,8]naphthyridine, indolo[1,2-b]-2,6-naphthyridine, indolo[1,2-b][2,7]naphthyridine, indolo[1,2-h]-1,7-naphthyridine, indolo[1,2-b]isoquinoline, indolo[1,2-a]isoquinoline, indolo[1,2-a]quinoline, 2H,6H-pyrido[2',1':3,4][1,4]diazepino[1,2-a]indole, 1H-indolo[2,1-c][1,4]benzodiazepine, 2H-indolo[1,2-d][1,4]benzodiazepine, 2H-indolo[2,1-a][2,3]benzodiazepine, 2H-indolo[2,1-b][1,3]benzodiazepine, 1H-indolo[1,2-b][2]benzazepine, 2H-indolo[1,2-a][1]benzazepine, 2H-indolo[2,1-a][2]benzazepine, indolo[1,2-

e][1,5]benzodiazocine, indolo[2,1-b][3]benzazocine, and the like.

The group of the above-mentioned formula:



[wherein each symbol has the same significance as mentioned above]

includes the groups derived from tetracyclic condensed benzene rings by removing one hydrogen atom, which are exemplified by 1H-imidazo[1',2':1,2]pyrido[3,4-b]indole, 1H-imidazo[1',2':1,6]pyrido[4,3-b]indole, 1H-imidazo[1',5':1,2]pyrido[3,4-b]indole, 1H-imidazo[1',5':1,6]pyrido[4,3-b]indole, 1H-imidazo-[2',1':2,3]pyrido[4,5-b]indole, imidazo[4,5-a]-carbazole, imidazo[4,5-c]carbazole, pyrazolo[3,4-c]carbazole, 2H-pyrazino[1',2':1,5]pyrrolo[2,3-b]indole, 1H-pyrrolo[1',2':1,2]pyrimido[4,5-b]indole, 1H-indolizino[6,7-b]indole, 1H-indolizino[8,7-b]indole, indolo[2,3-b]indole, indolo[3,2-b]indole, pyrrolo[2,3-a]carbazole, pyrrolo[2,3-b]carbazole, pyrrolo[2,3-c]carbazole, pyrrolo[3,2-a]carbazole, pyrrolo-[3,2-b]carbazole, pyrrolo[3,2-c]carbazole, pyrrolo[3,4-a]-carbazole, pyrrolo[3,4-b]carbazole, pyrrolo[3,4-c]carbazole, 1H-pyrido[3',4':4,5]furo[3,2-b]indole, 1H-furo[3,4-a]-carbazole, 1H-furo[3,4-b]carbazole, 1H-furo[3,4-c]carbazole,

2H-furo[2,3-a]carbazole, 2H-furo[2,3-c]carbazole, 2H-furo-[3,2-a]carbazole, 2H-furo[3,2-c]carbazole, 1H-pyrido[3',4':4,5]thieno[2,3-b]indole, thieno[3',2':5,6]thiopyrano[4,3-b]indole, thieno[3',4':5,6]thiopyrano[4,3-b]indole, 1H-[1]-benzothieno[2,3-b]indole, 1H-[1]-benzothieno[3,2-b]indole, 1H-thieno[3,4-a]carbazole, 2H-thieno[2,3-b]carbazole, 2H-thieno[3,2-a]carbazole, 2H-thieno[3,2-b]carbazole, cyclopenta[4,5]pyrrolo[2,3-f]quinoxaline, cyclopenta[5,6]pyrido[2,3-b]indole, pyrido[2',3':3,4]cyclopenta[1,2-b]indole, pyrido[2',3':4,5]cyclopenta[1,2-b]indole, pyrido[3',4':3,4]cyclopenta[1,2-b]indole, pyrido[3',4':4,5]cyclopenta[1,2-b]indole, pyrido[4',3':4,5]cyclopenta[1,2-b]indole, 1H-cyclopenta[5,6]pyrano[2,3-b]indole, 1H-cyclopenta[5,6]thio-pyrano[4,3-b]indole, cyclopenta[a]carbazole, cyclopenta[c]-carbazole, indeno[1,2-b]indole, indeno[2,1-b]indole, [1,2,4]triazino[4',3':1,2]pyrido[3,4-b]indole, 1,3,5-triazino[1',2':1,1]pyrido[3,4-b]indole, 1H-[1,4]oxazino-[4',3':1,2]pyrido[3,4-b]indole, 1H-[1,4]oxazino[4',3':1,6]-pyrido[3,4-b]indole, 4H-[1,3]oxazino[3',4':1,2]pyrido[3,4-b]indole, indolo[3,2-b][1,4]benzoxazine, 1,3-oxazino[6,5-b]carbazole, 2H-pyrimido[2',1':2,3][1,3]thiazino[5,6-b]indole, 2H-[1,3]thiazino[3',2':1,2]pyrido[3,4-b]indole,

4H-[1,3]thiazino[3',4':1,2]pyrido[3,4-b]indole, indolo[2,3-b][1,4]benzothiazine, indolo[3,2-b][1,4]benzothiazine, indolo[3,2-c][2,1]benzothiazine, 1,4-thiazino[2,3-a]carbazole, [1,4]-thiazino[2,3-b]carbazole, [1,4]thiazino[2,3-c]carbazole, 1,4-thiazino[3,2-b]carbazole, 1,4-thiazino[3,2-c]carbazole, 1H-indolo[2,3-g]pteridine, 1H-indolo[3,2-g]pteridine, pyrazino[1',2':1,2]pyrido[3,4-b]indole, pyrazino[1',2':1,2]pyrido[4,3-b]indole, 1H-pyrido[2',3':5,6]pyrazino[2,3-b]indole, 1H-pyrido[3',2':5,6]pyrazino[2,3-b]indole, 1H-pyrido[3',4':5,6]pyrazino[2,3-b]indole, pyrido[1',2':1,2]-pyrimido[4,5-b]indole, pyrido[1',2':1,2]pyrimido[5,4-b]-indole, pyrido[2',1':2,3]pyrimido[4,5-b]indole, pyrido-[1',2':1,2]pyrido[3,4-b]indole, pyrimido[1',2':1,6]pyrido-[3,4-b]indole, pyrimido[5',4':5,6]pyrano[2,3-b]indole, pyridazino[4',5':5,6]thiopyrano[4,5-b]indole, 1H-indolo-[3,2-c]cinnoline, 1H-indolo[2,3-b]quinoxaline, 1H-pyrazino-[2,3-a]carbazole, 1H-pyrazino[2,3-b]carbazole, 1H-pyrazino-[2,3-c]carbazole, 1H-pyridazino[3,4-c]carbazole, 1H-pyridazino[4,5-b]carbazole, 1H-pyrimido[4,5-a]carbazole, 1H-pyrimido[4,5-c]carbazole, 1H-pyrimido[5,4-a]carbazole, 1H-pyrimido[5,4-b]carbazole, 1H-pyrimido[5,4-c]carbazole, 7H-1,4-dioxino[2',3':5,6][1,2]dioxino[3,4-b]indole, 6H-[1,4]benzodioxino[2,3-b]indole, 6H-[1,4]benzodithiino[2,3-b]indole, 1H-indolo[2,3-b]-1,5-naphthyridine, 1H-indolo-

[2,3-b][1,6]naphthyridine, 1H-indolo[2,3-b][1,8]naphthyridine, 1H-indolo[2,3-c]-1,5-naphthyridine, 1H-indolo[2,3-c][1,6]naphthyridine, 1H-indolo[2,3-c][1,7]naphthyridine, 1H-indolo[2,3-c][1,8]naphthyridine, 1H-indolo[3,2-b]-1,5-naphthyridine, 1H-indolo[3,2-b][1,7]naphthyridine, 1H-indolo[3,2-b][1,8]naphthyridine, 1H-indolo[3,2-c][1,8]naphthyridine, indolo[2,3-a]quinolizine, indolo[2,3-b]quinolizine, indolo[3,2-a]quinolizine, indolo[3,2-b]quinolizine, pyrano[4',3':5,6]pyrido[3,4-b]indole, pyrido[4',3':4,5]pyrano[3,2-b]indole, pyrido[4',3':5,6]pyrano[2,3-b]indole, pyrido[4',3':5,6]pyrano[3,4-b]indole, 1H-indolo[2,3-c]isoquinoline, 1H-indolo[3,2-c]isoquinoline, 1H-indolo[2,3-c]quinoline, 1H-indolo[3,2-c]quinoline, 1H-pyrido[2,3-a]carbazole, 1H-pyrido[2,3-b]carbazole, 1H-pyrido[2,3-c]carbazole, 1H-pyrido[3,2-a]carbazole, 1H-pyrido[3,2-b]carbazole, 1H-pyrido[3,2-c]carbazole, 1H-pyrido[3,4-a]carbazole, 1H-pyrido[3,4-b]carbazole, 1H-pyrido[3,4-c]carbazole, 1H-pyrido[4,3-a]carbazole, 1H-pyrido[4,3-b]carbazole, 1H-pyrido[4,3-c]carbazole, 1H-quindoline, 1H-quinindoline, 1H-pyrano[3',4':5,6]pyrano[4,3-b]indole, [1]-benzopyrano[2,3-b]indole, [1]benzopyrano[3,2-b]indole, [1]-benzopyrano[3,4-b]indole, [1]benzopyrano[4,3-b]indole, [2]-benzopyrano[4,3-b]indole, pyrano[2,3-a]carbazole, pyrano[2,3-b]carbazole,

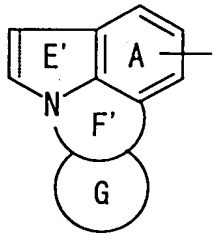
pyrano[2,3-c]carbazole, pyrano[3,2-a]-carbazole, pyrano[3,2-c]carbazole, pyrano[3,4-a]carbazole, 1H-phosphinolino[4,3-b]indole, [1]benzothiopyrano[2,3-b]indole, [1]benzothiopyrano[3,2-b]indole, [1]benzothiopyrano[3,4-b]indole, [1]benzothiopyrano[4,3-b]indole, [2]benzothiopyrano[4,3-b]indole, 1H-benzo[a]carbazole, 1H-benzo[b]carbazole, 1H-benzo[c]carbazole, [1,6,2]oxathiazepino[2',3':1,2]pyrido[3,4-b]indole, 1H-azepino[1',2': 1,2]pyrido[3,4-b]indole, 1H-pyrido[1',2':1,2]azepino[4,5-b]indole, 2H-pyrido[1',2':1,2]azepino[3,4-b]indole, 1H-pyrido[3',2':5,6]oxepino[3,2-b]indole, 1H-pyrido[4',3':5,6]oxepino[3,2-b]indole, 2H-pyrido[2',3':5,6]oxepino[2,3-b]indole, 2H-pyrido[2',3':5,6]oxepino[3,2-b]indole, 2H-pyrido-[3',4':5,6]oxepino[3,2-b]indole, pyrido[2',3':4,5]cyclohepta[1,2-b]indole, pyrido[3',2':3,4]cyclohepta[1,2-b]indole, pyrido[3',4':4,5]cyclohepta[1,2-b]indole, pyrido[3',4':5,6]cyclohepta[1,2-b]indole, 2H-pyrano[3',2':2,3]azepino[4,5-b]indole, 1H-indolo[3,2-b][1,5]benzoxazepine, 1H-indolo[3,2-d][1,2]benzoxazepine, 1H-indolo[2,3-c][1,5]benzothiazepine, [1,4]diazepino[2,3-a]carbazole, indolo[2,3-b][1,5]benzodiazepine, indolo[2,3-d][1,3]benzodiazepine, indolo[3,2-b][1,4]benzodiazepine,

indolo[3,2-b][1,5]benzodiazepine, indolo[3,2-d][1,3]benzodiazepine, indolo[3,2-d][2,3]benzodiazepine, indolo[2,3-a][3]benzazepine, indolo[2,3-c][1]benzazepine, indolo[2,3-d][1]benzazepine, indolo[2,3-d][2]benzazepine, indolo[3,2-b][1]benzazepine, indolo[3,2-c][1]benzazepine, indolo[3,2-d][1]benzazepine, 1H-indolo[2,1-b][3]benzazepine, 1H-[1]benzoxepino[5,4-b]indole, 1H-[2]benzoxepino[4,3-b]indole, 1H-[1]benzothiepino[4,5-b]-indole, 1H-[1]benzothiepino[5,4-b]indole, benzo[3,4]cyclohepta[1,2-b]indole, benzo[4,5]cyclohepta[1,2-b]indole, benzo[5,6]cyclohepta[1,2-b]indole, benzo[6,7]cyclohepta[1,2-b]indole, cyclohepta[b]carbazole, 4H-[1,5]oxazocino[5',4':1,6]pyrido[3,4-b]indole, azocino[1',2':1,2]pyrido[3,4-b]indole, 2,6-methano-2H-azecino[4,3-b]indole, 3,7-methano-3H-azecino-[5,4-b]indole, pyrido[1',2':1,8]azocino[5,4-b]indole, pyrido-[4',3':6,7]oxocino[2,3-b]indole, pyrido-[4',3':6,7]oxocino[4,3-b]indole, 1,5-methano-1H-azecino[3,4-b]indole, 2,6-methano-1H-azecino[5,4-b]indole, 1H-pyrido[3',4':5,6]cycloocta[1,2-b]indole, 1,4-ethanooxocino[3,4-b]indole, pyrano[3',4':5,6]cycloocta[1,2-b]indole, 1H-indolo[2,3-c][1,2,5,6]benzotetrazocine, 1H-indolo[2,3-c][1,6]benzodiazocine, 6,13b-methano-13bH-azecino[5,4-b]indole, oxocino[3,2-a]carbazole, 1H-benzo[g]cycloocta[b]indole, 6,3-(iminomethano)-2H-1,4-

thiazonino[9,8-b]indole, 1H,3H-[1,4]oxazonino[4',3':1,2]pyrido[3,4-b]indole, 2H-3,6-ethanoazonino[5,4-b]indole, 2H-3,7-methanoazacycloundecino[5,4-b]indole, 1H-6,12b-ethanoazonino[5,4-b]indole, indolo[3,2-e][2]benzazonine, 5,9-methanoazacycloundecino[5,4-b]indole, 3,6-ethano-3H-azecino[5,4-b]indole, 3,7-methano-3H-azacycloundecino[5,4-b]indole, pyrano[4',3':8,9]azecino[5,4-b]-indole, 1H-indolo[2,3-c][1,7]benzodiazecine, 1H-indolo[3,2-e][2]benzazecine, benzo[e]pyrrolo[3,2-b]indole, benzo[e]-pyrrolo[3,2-g]indole, benzo[e]pyrrolo[3,2,1-hi]indole, benzo[e]pyrrolo[3,4-b]indole, benzo[g]pyrrolo[3,4-b]indole, 1H-benzo[f]pyrrolo[1,2-a]indole, 1H-benzo[g]pyrrolo[1,2-a]indole, 2H-benzo[e]pyrrolo[1,2-a]indole, 1H-benzo[f]-pyrrolo[2,1-a]isoindole, 1H-benzo[g]pyrrolo[2,1-a]isoindole, 2H-benzo[e]pyrrolo[2,1-a]isoindole, isoindolo[6,7,1-cde]-indole, spiro[cyclohexane-1,5'-[5H]pyrrolo[2,1-a]isoindole], isoindolo[7,1,2-hij]quinoline, 7,11-methanoazocino[1,2-a]-indole, 7,11-methanoazocino[2,1-a]isoindole, dibenz[cd,f]-indole, dibenz[cd,g]indole, dibenz[d,f]indole, 1H-dibenz-[e,g]indole, 1H-dibenz[e,g]isoindole, naphtho[1,2,3-cd]-indole, naphtho[1,8-ef]indole, naphtho[1,8-fg]indole, naphtho[3,2,1-cd]indole, 1H-naphtho[1,2-e]indole, 1H-naphtho[1,2-f]indole, 1H-naphtho[1,2-g]indole, 1H-naphtho-[2,1-e]indole, 1H-naphtho[2,3-e]indole, 1H-naphtho[1,2-f]-

isoindole, 1H-naphtho[2,3-e]isoindole, spiro[1H-carbazole-1,1'-cyclohexane], spiro[2H-carbazol-2,1'-cyclohexane], spiro[3H-carbazol-3,1'-cyclohexane], cyclohepta[4,5]pyrrolo[3,2-f]quinoline, cyclohepta[4,5]pyrrolo[3,2-h]quinoline, azepino[4,5-b]benz[e]indole, 1H-azepino[1,2-a]benz[f]indole, 1H-azepino[2,1-a]benz[f]isoindole, benzo[e]cyclohepta[b]-indole, benzo[g]cyclohepta[b]indole, and the like.

The group of the above-mentioned formula:

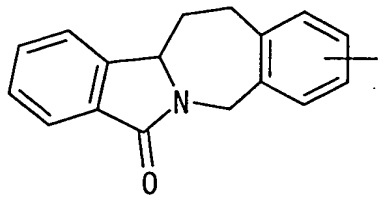


[wherein each symbol has the same significance as mentioned above]

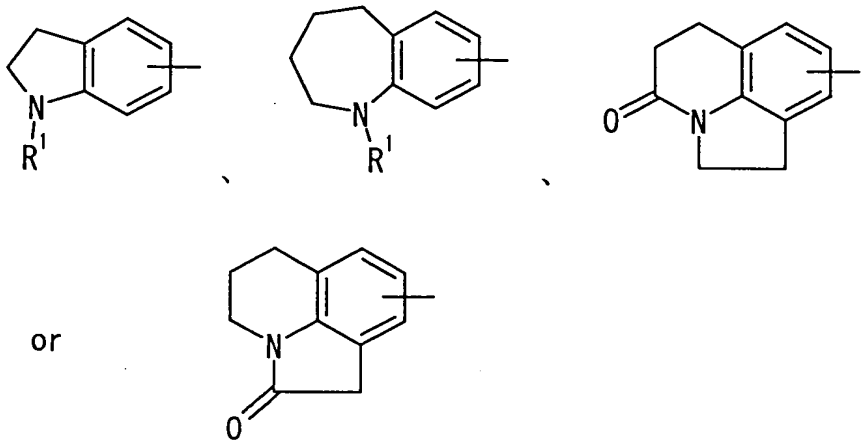
includes the groups derived from tetracyclic condensed benzene rings by removing one hydrogen atom, which are exemplified by 1H-dipyrrolo[2,3-b:3',2',1'-hi]indole, spiro[cyclopentane-1,2'(1'H)-pyrrolo[3,2,1-hi]indole], spiro[imidazolizine-4,1'(2'H)-[4H]pyrrolo[3,2,1-ij]quinoline], pyrido[2,3-b]pyrrolo[3,2,1-hi]indole, pyrido[4,3-b]pyrrolo[3,2,1-hi]indole, benzo[de]pyrrolo[3,2,1-ij]quinoline, 3H-pyrrolo[3,2,1-de]acridine, 1H-pyrrolo[3,2,1-de]phenanthridine, spiro[cyclohexane-1,6'-[6H]pyrrolo[3,2,1-ij]quinoline],

4,9-methanopyrrolo[3,2,1-lm][1]benzazocine, spiro[cycloheptane-1,6'-[6H]pyrrolo[3,2,1-ij]quinoline], 1H-pyrrano[3,4-d]pyrrolo[3,2,1-jk][1]benzazepine, 3H-benzo[b]pyrrolo[3,2,1-jk][4,1]benzoxazepine, 7H-indolo[1,7-ab][4,1]benzoxazepine, benzo[b]pyrrolo[3,2,1-jk][1,4]benzodiazepine, indolo[1,7-ab][1,4]benzodiazepine, indolo[1,7-ab][1]benzazepine, indolo[7,1-ab][3]benzazepine, 1H-cyclohepta[d][3,2,1-jk][1]benzazepine, spiro[azepino[3,2,1-hi]indole-7(4H),1'-cycloheptane], 4H-5,11-methanopyrrolo[3,2,1-no][1]benzazacycloundecine, spiro[azepino[3,2,1-hi]indole-7(4H),1'-cyclooctane], and the like.

Among them, particularly preferred is a group of the formula:

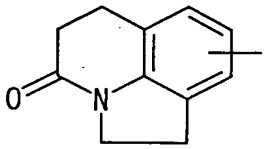


The "optionally condensed phenyl which may have a substituent or substituents" represented by Ar preferably includes, for example, optionally substituted groups of formula:



or

Particularly preferred is a group of formula:



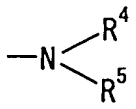
n is, preferably, an integer of 1 to 6. Particularly preferred are 2 to 6, and especially preferred is 2.

R is hydrogen or optionally substituted hydrocarbon group, which may be different according to repetition of n.

As for the "optionally substituted hydrocarbon group" represented by R, the same as in "optionally substituted hydrocarbon group" represented by R^1 may be exemplified.

R is preferably a hydrogen atom.

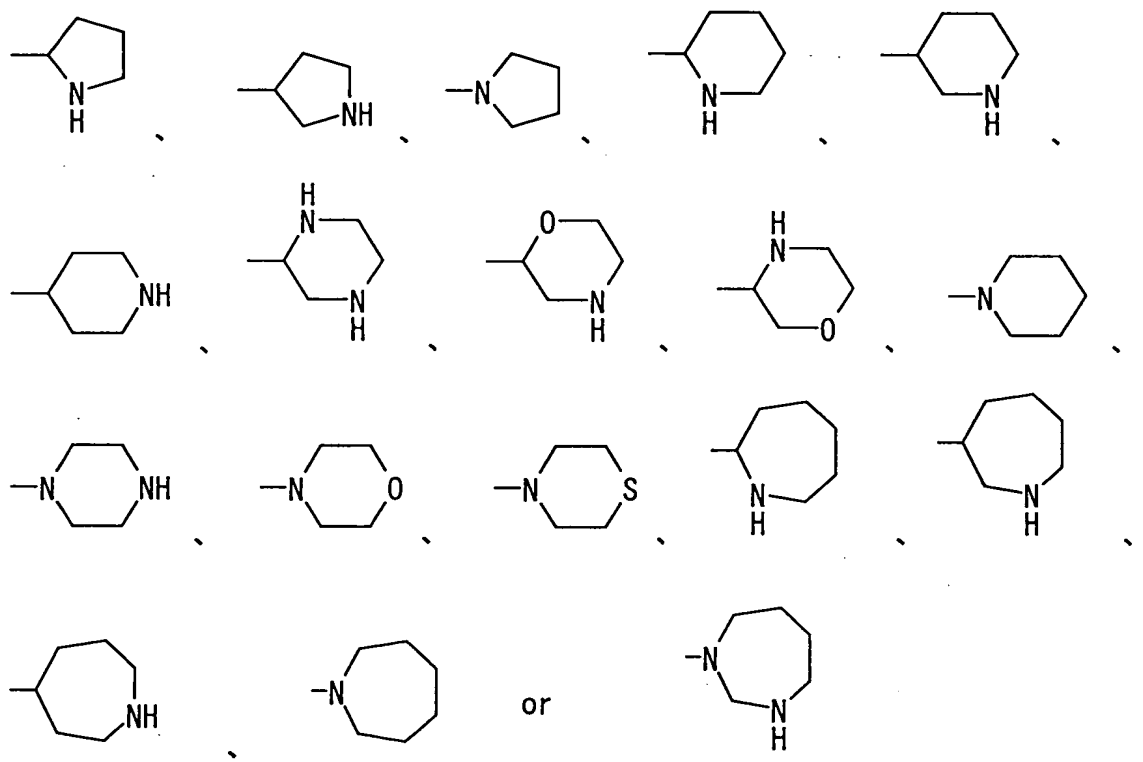
The "optionally substituted amino " represented by Y includes, for example, groups of the formula:



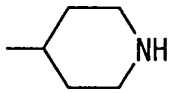
[wherein R^4 and R^5 each is hydrogen, optionally substituted hydrocarbon group, or acyl]

As for the "optionally substituted hydrocarbon group" and "acyl " represented by R^4 and R^5, the same as in "optionally substituted hydrocarbon group" and "acyl" represented by R^1 may be exemplified.

The "nitrogen-containing saturated heterocyclic group" of "optionally substituted nitrogen-containing saturated heterocyclic group" represented by Y includes 5- to 9-membered (preferably, 5- to 7-membered) nitrogen-containing saturated heterocyclic group which may contain 1 to 3 heteroatoms selected from nitrogen, oxygen and sulfur, in addition to carbon atoms and one nitrogen atom. Such a group is exemplified, for example, by groups of the formula:



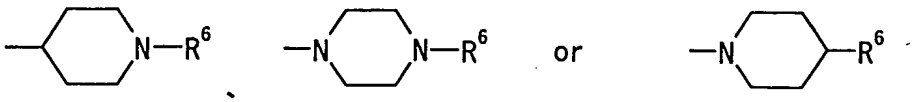
Among them, the 6-membered cyclic groups are preferred. Particularly preferred is a group of the formula:



As for the "substituent" of "optionally substituted nitrogen-containing saturated heterocyclic group", the same"substituent" as in "optionally substituted nitrogen-containing saturated heterocyclic group" represented by the above-mentioned ring B may be exemplified. The number of the substituent is 1 to 5. In addition, the nitrogen atom on the "nitrogen-containing saturated heterocyclic group" of "optionally substituted nitrogen-containing saturated heterocyclic group" may have

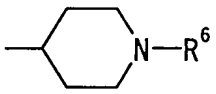
the same group as those represented by the above-mentioned R^1.

Preferably, Y is a group of the formula:



[wherein R^6 has the same significance as R^1]

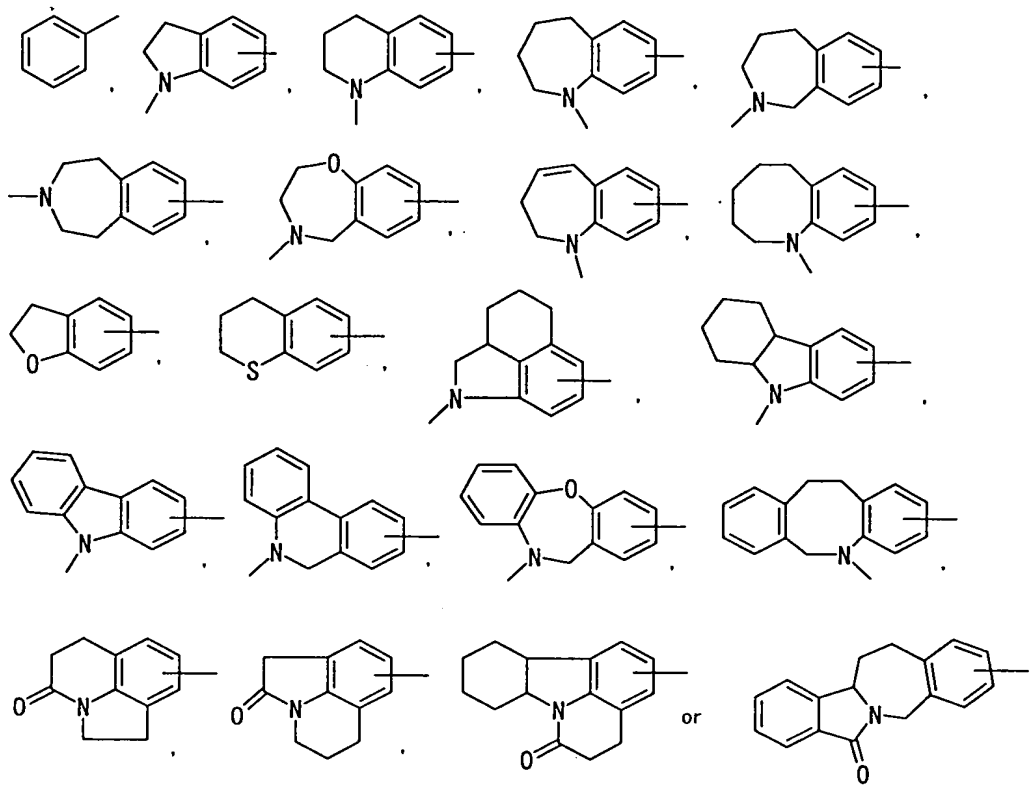
Particularly preferred is a group of the formula:



[wherein R^6 has the same significance as mentioned above]

R^6 is preferably hydrogen or optionally substituted hydrocarbon group. Particularly preferred are C_{7-16} aralkyl (preferably, benzyl) and the like, which may be substituted by 1 to 3 substituents selected from halogen (preferably, fluoro, etc.), C_{1-6} alkyl (preferably, methyl, etc.), C_{1-6} alkoxy (preferably, methoxy, etc.), cyano, nitro and hydroxy.

Compound (I) preferably includes those in which Ar is a group of the formula:



among which, when Ar is phenyl, it may be substituted by substituent(s) selected from (1) halogen (fluoro, etc.), (2) C_{1-6} alkoxy (methoxy, etc.), (3) amino, (4) (mono- or di-)C_{1-6} alkylamino (methylamino, ethylamino, dimethylamino, diethylamino, etc.), (5) pyrrolidino, (6) piperidino, (7) piperazino, (8) N-methylpiperazino, (9) N-acetylpiperazino, (10) morpholino, (11) hexamethylenimino, (12) imidazolyl, and (13) C_{1-6} alkyl (propyl, etc.) which may be substituted by a carboxy optionally esterified by C_{1-6} alkyl (methyl, etc.);

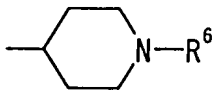
when Ar is condensed phenyl, its heterocyclic portion may be substituted by substituent(s) selected from (1) C_{1-6} alkyl (methyl, ethyl, propyl, n-butyl, etc.), (2)

C_{7-16} aralkyl (benzyl, phenyethyl, etc.) which may be substituted by substituent(s) selected from halogen (fluoro, chloro, etc.), C_{1-6} alkyl (methyl, etc.), C_{1-6} alkoxy (methoxy, etc.) and nitro, (3) C_{1-6} alkyl-carbonyl (acetyl, propionyl, isobutyryl, pivaloyl, etc.), (4) C_{7-16} aralkyl-carbonyl (phenylacetyl, etc.), (5) C_{6-14} aryl-carbonyl (benzoyl, etc.), (6) C_{1-6} alkyl-carbonyl-C_{6-14} aryl (methylbenzoyl, etc.), (7) C_{1-6} alkoxy-carbonyl-C_{6-14} aryl (methoxybenzoyl, etc.) and (8) pyridyl;

n is 2;

R is hydrogen;

Y is a group of the formula:



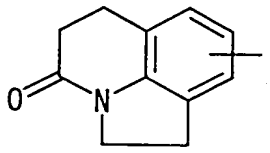
wherein the symbol has the same significance as mentioned above;

and

R^6 is (1) hydrogen atom, (2) C_{1-6} alkyl (methyl, ethyl, isopropyl, etc.) which may have substituent(s) selected from cyano, hydroxy, (mono- or di-)C_{1-6} alkylamino (diethylamino, etc.), pyridyl, and carboxy optionally esterified (by C_{1-6} alkyl (ethyl, etc.)), (3) C_{7-16} aralkyl (benzyl, α-methylbenzyl, phenylethyl, etc.) which may be substituted by substituent(s) selected from halogen (fluoro, chloro, etc.), C_{1-6} alkyl (methyl, t-butyl, etc.), halogeno

C_{1-6} alkyl (trifluoromethyl, etc.), hydroxy, C_{1-6} alkoxy (methoxy, etc.), nitro, amino, cyano, carbamoyl, C_{1-6} alkoxy optionally substituted by carboxy (OCH_2CO_2H, OCH_2CO_2Et, etc.) which may be esterified (by C_{1-6} alkyl, etc.), carbamoyl optionally substituted by C_{1-6} alkyl or amino optionally substituted by formyl (NHCHO, $NHCONH_2$, NHCONHMe, etc.), and C_{1-3} alkylenedioxy (methylenedioxy, etc.), (4) C_{1-6} alkyl (methyl, propyl, etc.) which may be substituted by carboxy optionally esterified (by C_{1-6} alkyl (ethyl, etc.), etc.), or (5) C_{1-6} alkyl-carbonyl (acetyl, etc.) optionally substituted by (mono- or di-)C_{1-6} alkylamino (dimethylamino, etc.).

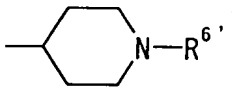
Particularly preferred Compound (I) includes those in which Ar is a group of the formula:



n is 2;

R is hydrogen;

Y is a group of the formula:



[wherein $R^{6'}$ is benzyl which may be substituted by 1 or 2 substituents selected from halogen, C_{1-3} alkyl, C_{1-3} alkoxy, cyano, nitro and hydroxy]

Particularly preferred are:

8-[3-[1-[(3-fluorophenyl)methyl]-4-piperidinyl]-1-oxopropyl]-1,2,5,6-tetrahydro-4H-pyrrolo[3,2,1-ij]quinolin-4-one;

8-[3-[1-(phenylmethyl)-4-piperidinyl]-1-oxopropyl]-1,2,5,6-tetrahydro-4H-pyrrolo[3,2,1-ij]quinolin-4-one; and

8-[3-[1-[(2-hydroxyphenyl)methyl)-4-piperidinyl]-1-oxopropyl]-1,2,5,6-tetrahydro-4H-pyrrolo[3,2,1-ij]quinolin-4-one;

or salts thereof.

Compounds (I) or salts thereof may be produced by a per se known process or its equivalent process. For example, the objective compounds of the above formula may be produced according to:

(1) the methods as described in JP-A 3-173867/1991 (EP-A 0378207) and JP-A 64-79151/1989 (EP-A 0296560), when the "optionally condensed phenyl which may be substituted by a substituent or substituents" represented by Ar does not form a condensed ring;

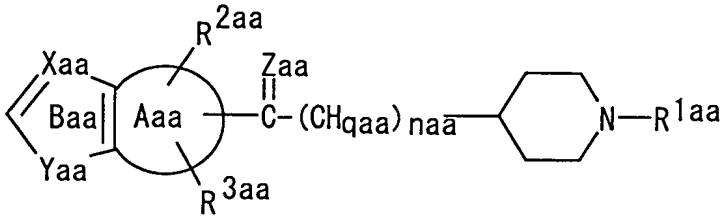
(2) the methods as described in JP-A 5-140149/1993 (EP-A 0487071), JP-A 6-166676/1994 (EP-A 0560235), JP-A 6-206875/1994 (EP-A 0567090), and JP-A 2-169569/1990 (USP 4,895,841), when the "optionally condensed phenyl which may be substituted by a substituent or

substituents" represented by Ar is condensed with an optionally substituted monocyclic heterocycle;

(3) the methods as described in JP-A 7-206854/1995 (EP-A 0607864), when the "optionally condensed phenyl which may be substituted by a substituent or substituents" represented by Ar is condensed with an optionally substituted bicyclic heterocycle or with two identical or different monocyclic heterocycle (provided that at least one of two is a monocyclic heterocycle); and

(4) the methods as described in JP-A 7-309835/1995 (EP-A 0655451), when the "optionally condensed phenyl which may be substituted by a substituent or substituents" represented by Ar is condensed with an optionally substituted tricyclic heterocycle.

2) Compounds of the formula:



wherein one of the side chain containing C=Zaa, R^{2aa} and R^{3aa} is attached to the carbon atom indicated by an asterisk * on the ring Baa; the ring Aaa is benzo, thieno, pyrido, pyrazino, pyrimido, furano, seleno, pyrrolo, thiazolo or imidazolo; R^{1aa} is phenyl, phenyl-C_{1-6} alkyl, cinnamyl or heteroarylmethyl (where the heteroaryl includes imidazolo,

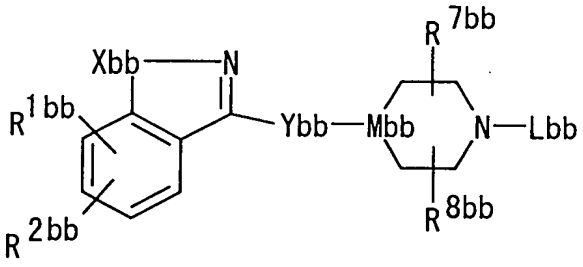
thiazolo, thieno, pyrido or isoxazolo), and the phenyl and heteroaryl may be substituted by 1 or 2 substituents selected from C_{1-6} alkyl, C_{1-6} alkoxy and halogen; R^{2aa} and R^{3aa} each represents independently a hydrogen atom, C_{1-6} alkoxy, C_{1-6} alkyl optionally substituted by 1 - 3 fluorine atoms, benzyloxy, hydroxy, phenyl, benzyl, halogen, nitro, cyano, $COOR^{4aa}$, $CONHR^{4aa}$, $NR^{4aa}R^{5aa}$, $NR^{4aa}COR^{5aa}$ or $SOpaaCH_2Ph$ (where paa is 0, 1 or 2), or R^{2aa} and R^{3aa} taken with the adjacent carbon atoms may form a 5- or 6-membered ring (carbon, nitrogen and oxygen atoms constitutes the ring), for example, methylenedioxy, ethylenedioxy or lactam ring; R^{4aa} and R^{5aa} each represents independently hydrogen or C_{1-6} alkyl, or R^{4aa} and R^{5aa} in $NR^{4aa}R^{5aa}$ taken with the adjacent nitrogen atom may form a 4- to 8-membered ring containing at least one nitrogen atom (the other atoms constituting the ring are carbon, oxygen and nitrogen); in addition, R^{4aa} and R^{5aa} in $NR^{4aa}COR^{5aa}$ taken with the adjacent nitrogen atom and carbon atom may form a 4- to 8-membered lactam ring; Xaa is nitrogen or CH, and Yaa is oxygen, sulfur or NR^{6aa}; R^{6aa} is hydrogen, C_{1-6} alkyl, $CO-C_{1-6}$ alkyl or SO_2-phenyl (where the phenyl may be substituted by 1 to 5 substituents independently selected from C_{1-4} alkyl); naa is an integer of 1 to 4; qaa each is independently 1 or 2; Zaa is oxygen or sulfur;

or salts thereof. Such compounds are exemplified by 1-(2-

methyl-1H-benzimidazol-5-yl)-3-[1-(phenylmethyl)-4-piperidinyl]-1-propanone, 1-(6-methylbenzo[b]thien-2-yl)-3-[1-(phenylmethyl)-4-piperidinyl]-1-propanone, 1-(6-methyl-indol-2-yl)-3-[1-(phenylmethyl)-4-piperidinyl]-1-propanone, and the like.

The above-mentioned compounds or salts thereof may be produced according to the process as described in WO 93/07140 or its equivalent process.

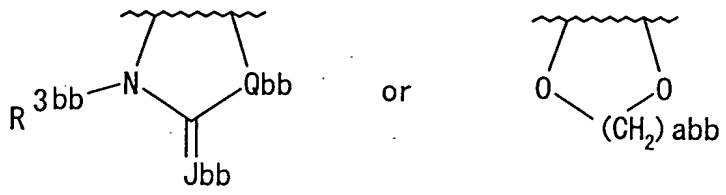
3) Compounds of the formula:



wherein R^{1bb} and R^{2bb} each is hydrogen, C_{1-6} alkoxy, benzyloxy, phenoxy, hydroxy, phenyl, benzyl, halogen, nitro, cyano, group of the formula: COR^{5bb}, $-COOR^{5bb}$, $-CONHR^{5bb}$, $-NR^{5bb}R^{6bb}$ or $-NR^{5bb}COR^{6bb}$ (where R^{5bb} and R^{6bb} each is i] hydrogen atom, ii] C_{1-6} alkyl, iii] phenyl or benzyl which may be substituted by 1 or 2 substituents selected from halogen, C_{1-4} alkyl, trifluoromethyl, C_{1-4} alkoxy, cyano, nitro and hydroxy; or R^{5bb} and R^{6bb} in $-NR^{5bb}R^{6bb}$ taken together may form a 4- to 8-membered nitrogen-containing ring; R^{5bb} and R^{6bb} in $-NR^{5bb}COR^{6bb}$ taken together may form a 4- to 8-membered lactam ring], C_{1-6} alkyl optionally substituted by 1 to 3 fluorine atoms,

group of the formula: $SO_{pbb}CH_2$-phenyl or $SO_{pbb}C_{1-6}$ alkyl (where pbb is 0, 1 or 2), pyridylmethyloxy, thienylmethyloxy, 2-oxazolyl, 2-thiazolyl or benzenesulfonamido (said phenoxy, benzyloxy, phenyl, benzyl, benzenesulfonamido, pyridylmethyloxy, thienylmethyloxy, 2-oxazolyl, and 2-thiazolyl may be substituted by 1 or 2 sub-stituents selected from halogen, C_{1-6} alkyl, trifluoromethyl, C_{1-6} alkoxy, cyano, nitro and hydroxy); or

R^{1bb} and R^{2bb}, when they are attached to the adjacent carbon atoms and when Xbb is oxygen, sulfur or NR^{4bb} (R^{4bb} is hydrogen or C_{1-4} alkyl), taken with the attached carbon atoms may form a group of the formula:



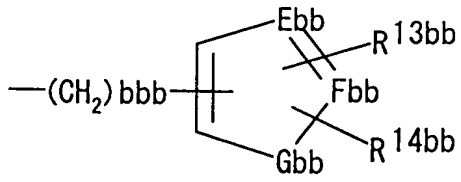
[wherein Jbb is oxygen, sulfur or NR^{4bb}; abb is 1 or 2; R^{3bb} is hydrogen or C_{1-6} alkyl; Qbb is oxygen, sulfur, NH, $CHCH_3$, $C(CH_3)_2$, -CH=CH- or $(CH_2)_{1bb}$; and 1bb is an integer of 1 to 3];

Xbb is oxygen, sulfur, -CH=CH-, -CH=N-, -NH=CH-, -N=N- or NR^{4bb} (R^{4bb} has the same significance as mentioned above);

Ybb is $-(CH_2)_{mbb}-$, $-CH=CH(CH_2)_{nbb}-$, $-NR^{4bb}(CH_2)_{mbb}-$ or $-O(CH_2)_{mbb}-$ (R^{4bb} has the same significance as mentioned above; nbb is an integer of 0 to 3; mbb is an integer of 1 to 3);

Mbb is -CH- or nitrogen;

Lbb is i) phenyl or phenyl-C_{1-6} alkyl which may be substituted by 1 to 3 substituents selected from halogen, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkoxy-carbonyl and C_{1-6} alkyl-carbonyl, ii) cinnamyl, iii) pyridylmethyl, or iv) group of the formula:



[wherein bbb is an integer of 1 to 4; R^{13bb} and R^{14bb} each is hydrogen, C_{1-4} alkyl, halogen or phenyl; Ebb and Fbb each is -CH- or nitrogen; Gbb is oxygen, sulfur or NR^{4bb} (R^{4bb} has the same significance as mentioned above); provided that when both of Ebb and Fbb are nitrogen, then one of R^{13bb} and R^{14bb} is absent]

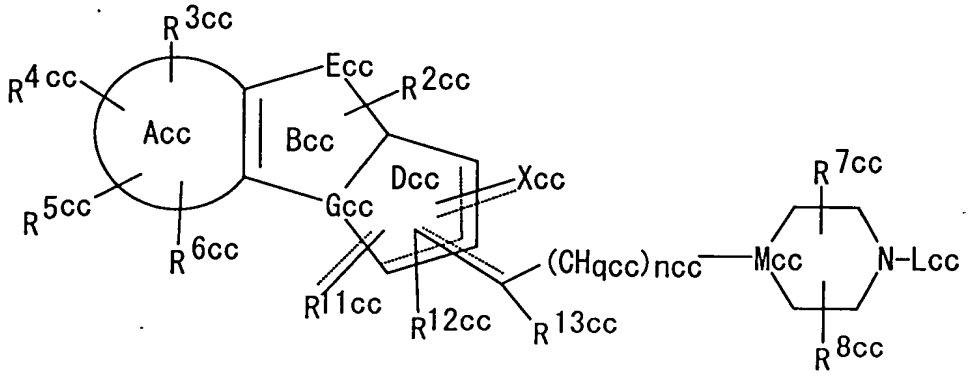
R^{7bb} and R^{8bb} each is hydrogen, C_{1-6} alkyl, C_{1-6} alkoxy-carbonyl, C_{1-6} alkyl-carbonyl, or C_{1-6} alkoxy; provided that said C_{1-6} alkoxy is not attached to the carbon atom adjacent to the nitrogen]

or salts thereof. Such compounds are exemplified by 3-[2-[1-(phenylmethyl)-4-piperidinyl]ethyl]-5,6,8-trihydro-7H-isoxazolo[4,5-g]quinolin-7-one, 6,8-dihydro-3-[2-[1-(phenylmethyl)-4-piperidinyl]ethyl]-7H-pyrrolo[5,4-g]-1,2-benzisoxazol-7-one, 5,7-dihydro-3-[2-[1-(phenylmethyl)-4-piperidyl]ethyl]-6H-pyrrolo[5,4-f]-1,2-benzisoxazol-6-one,

and the like.

The above-mentioned compounds or salts thereof may be produced according to the process as described in PCT JP-A 6-500794/1994 (WO 92/17475) or its equivalent process.

4) Compounds of the formula:



[wherein the ring Acc is benzo, thieno, pyrido, pirazino, pyrimido, furano, seleno or pyrrolo;

R^{2cc} is hydrogen, C_{1-4} alkyl, benzyl, fluoro or cyano;

R^{3cc}, R^{4cc}, R^{5cc} and R^{6cc} each is hydrogen, C_{1-6} alkoxy, benzyloxy, phenoxy, hydroxy, phenyl, benzyl, halogen, nitro, cyano, $-COOR^{9cc}$, $-CONHR^{9cc}$, $-NR^{9cc}R^{10cc}$, $-NR^{9cc}COR^{10cc}$, or C_{1-6} alkyl which may be substituted by 1 to 3 fluorine atoms; $SO_{pcc}CH_2$-phenyl (pcc is 0, 1 or 2), pyridylmethyloxy or thienylmethyloxy (said phenoxy, benzyloxy, phenyl, pyridylmethyloxy and thienylmethyloxy may be substituted by 1 or 2 substituents selected from halogen, C_{1-4} alkyl, trifluoromethyl, C_{1-4} alkoxy, cyano, nitro and hydroxy); or two of R^{3cc}, R^{4cc}, R^{5cc} and R^{6cc}, taken with the adjacent carbon

atoms, may form a saturated 5- or 6-membered ring (e.g., methylenedioxy, ethylenedioxy or lactam ring) in which each atom is carbon, nitrogen or oxygen in additon to the adjacent carbon atoms;

R^{9cc} and R^{10cc} each is hydrogen or C_{1-6} alkyl; or

R^{9cc} and R^{10cc} in $NR^{9cc}R^{10cc}$ taken together may form a 4- to 8-membered cyclic amino in which one of the ring-constituting atoms is nitrogen and the others are carbon; or

R^{9cc} and R^{10cc} in $NR^{9cc}COR^{10cc}$ taken together may form a 4- to 8-membered lactam ring;

Gcc is carbon or nitrogen;

Ecc is carbon, nitrogen, oxygen, sulfur, sulfoxide or sulfone;

$\underline{\equiv}$ is a single bond or double bond;

the carbon located at any of the 1-, 2- or 3-position adjacent to a carbonyl group on the ring DCC may be replaced by an appropriate nitrogen (to form a lactam ring as said carbon is located at the 1-, 2- or 3-position on the ring DCC);

Xcc is O, S, NOR^{1cc}, hydrogen or C_{1-6} alkyl (provided that a double bond is formed between Xcc and the ring Dcc, only when the atom on the ring Dcc to which Xcc is attached is carbon, and Xcc is O, S or NOR^{1cc});

R^{1cc} is hydrogen or C_{1-6} alkyl;

qcc is 1 or 2;

when the ring Dcc is a lactam, ncc is an integer of 1 to 3, and when the ring Dcc is not lactam, ncc is 0 or an integer of 1 to 3;

Mcc is carbon or nitrogen;

Lcc is phenyl, phenyl-C_{1-6} alkyl, cinnamyl or pyridylmethyl (said phenyl and phenyl-C_{1-6} alkyl may be substituted by 1 to 3 substituents selected from C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkoxy- carbonyl, C_{1-6} alkyl-carbonyl and halogen);

R^{11cc} is hydrogen, halogen, hydroxy, C_{1-4} alkyl, C_{1-4} alkoxy or oxygen;

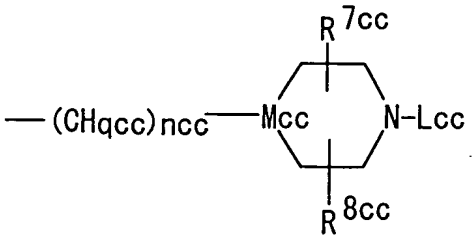
R^{12cc} and R^{13cc} each is hydrogen, fluoro, hydroxy, acetoxy, O-mesylate, O-tosylate, C_{1-4} alkyl or C_{1-4} alkoxy; or when both of R^{12cc} and R^{13cc} are attached to carbon atoms, they taken with the atoms to which they are attached may form a 3- to 5-membered ring in which the constituting atoms are carbon or oxygen;

R^{7cc} and R^{7cc} each is hydrogen, C_{1-6} alkyl or C_{1-6} alkoxy (said C_{1-6} alkoxy is not bound to the carbon adjacent to the nitrogen, C_{1-6} alkoxy-carbonyl and C_{1-6} alkyl-carbonyl); or

R^{8cc} and R^{12cc}, taken with the atoms to which they are attached, may form a 4- to 7-membered saturated carboycle (one of the above-mentioned carbon atoms may be replaced by oxygen, nitrogen or sulfur);

provided that (a) when Ecc is carbon, nitrogen, oxygen, sulfur, sulfoxido or sulfone, Gcc is carbon; (b) when Gcc

is nitrogen, Ecc is carbon or nitrogen; (c) when both of Ecc and Gcc are nitrogen, and when Gcc is carbon and Ecc is oxygen, sulfur, sulfoxido or sulfone, R^{2cc} is absent; (d) the atoms located at the 1-, 2- and 3-positions on the ring Dcc each is not bound through more than one double bond; (e) when R^{11cc} is oxygen, it is bound to the ring Dcc through a double bond, and when R^{11cc} is other than oxygen, it is bound to the ring Dcc by a single bond; (f) when Xcc and R^{11cc} both are oxygen and respectively bound to the carbon at the 1- and 3-positions or at the 3- and 1-positions on the ring Dcc, the carbon at the 2-position on the ring Dcc is replaced by nitrogen; and (g) Xcc is bound to the ring Dcc at the adjacent position at which a hydrocarbon group containing a group of the formula:



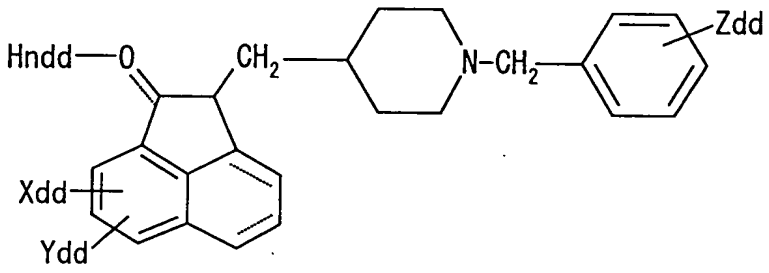
is attached]

or salts thereof. Such compounds are exemplified by 2,3-dihydro-2-[[1-(phenylmethyl)-4-piperidinyl]methylene]-1H-pyrrolo[1,2-a]indol-1-one, 1,2,3,4-tetrahydro-4-methyl-2-[[1-(phenylmethyl)-4-piperidinyl]methylene]-cyclopent[b]-indol-3-one, 2,3-dihydro-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-1H-pyrrolo[1,2-a]benzimidazol-1-one, 1,2,3,4-

tetrahydro-6-methyl-2-[[1-(phenylmethyl)-4-piperidinyl]-ethyl]pyrrolo[3,4-b]indol-3-one, and the like.

The above-mentioned compounds or salts thereof may be produced according to the process as described in JP-A 4-234845/1992 (EP-A 441517) or its equivalent process.

5) Compounds of the formula:

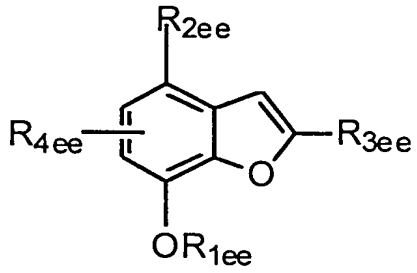


wherein Xdd is hydrogen, lower alkyl, lower alkoxy, hydroxy or nitro; Ydd is hydrogen or lower alkoxy; or Xdd and Ydd taken together form a group of $-OCH_2O-$ (in this case each position of Xdd and Ydd attached on the benzene ring has to be adjacent each other); Zdd is hydrogen, lower alkyl, lower alkoxy, hydroxy, halogen or nitro; ndd is 0 or 1; or salts thereof. Such compounds are exemplified by 2-[(N-benzylpiperidin-4-yl)methyl]-2a,3,4,5-tetrahydro-1(2H)-acenaphthylen-1-one, 2-[[N-(3-fluorobenzyl)piperidin-4-yl)methyl]-2a,3,4,5-tetrahydro-1(2H)-acenaphthylen-1-one, and the like.

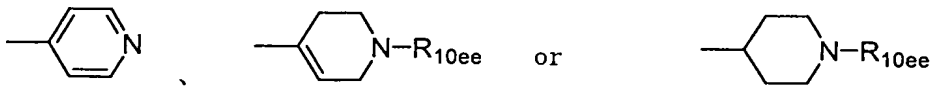
The above-mentioned compounds or salts thereof may be produced according to the process as described in JP-A 6-116237/1994 (EP-A 517221, USP 5,106,856) or its

equivalent process.

6) Compounds of the formula:



wherein R_{1ee} is hydrogen, lower alkyl, aryl lower alkyl, $CONHR_{11ee}$ or $CONR_{6ee}R_{7ee}$; R_{2ee} is hydrogen, cyano, $CH_2NR_{8ee}R_{9ee}$, $CONHR_{5ee}$ or $CONR_{6ee}R_{7ee}$; R_{3ee} is a group of the formula:



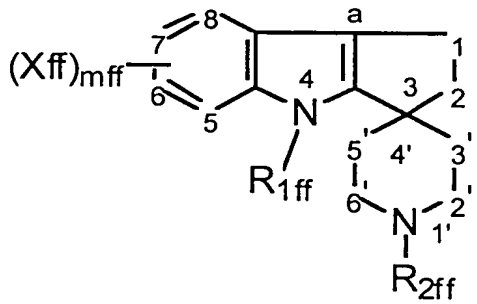
(where R_{10ee} is hydrogen, lower alkyl, aryl lower alkyl, $CONHR_{5ee}$, $CONR_{6ee}R_{7ee}$, acyl, acyloxy lower alkyl or acyloxy-aryl lower alkyl); R_{4ee} is hydrogen, halogen, lower alkyl or lower alkoxy; R_{5ee} is hydrogen, lower alkyl or aryl lower alkyl; R_{6ee} is lower alkyl or aryl lower alkyl; R_{7ee} is lower alkyl or aryl lower alkyl; R_{8ee} is hydrogen, lower alkyl, aryl lower alkyl or acyl; R_{9ee} is hydrogen, lower alkyl or aryl lower alkyl; R_{11ee} is lower alkyl, aryl or aryl lower alkyl; provided that when R_{1ee} is hydrogen or lower alkyl, R_{2ee} is not hydrogen;

or salts thereof. Such compounds are exemplified by 1-methyl-4-(4-cyano-7-methoxy-2-benzofuranyl)piperidine, 1-methyl-4-(4-N,N-diethylamido-7-methoxy-2-benzofuranyl)-

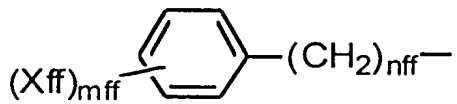
piperidine, 1-methyl-4-(4-N,N-diethylaminomethyl-7-methoxy-2-benzofuranyl)piperidine, and the like.

The above-mentioned compounds or salts thereof may be produced according to the process as described in JP-A 7-109275/1995 or its equivalent process.

7) Compounds of the formula:

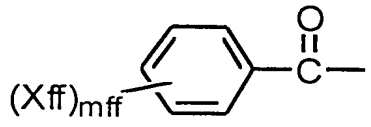


wherein Xff is hydrogen, halogen, lower alkoxy, lower alkyl, hydroxy or trifluoromethyl; mff is 1 or 2; R_{1ff} is hydrogen or lower alkyl; R_{2ff} is hydrogen, a group of the formula:



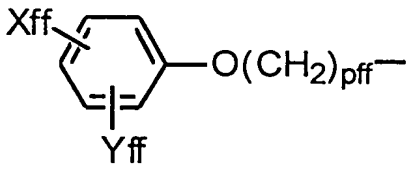
(wherein nff is 1 or 2; Xff and mff have the same significance as mentioned above),

a group of the formula:



(wherein Xff and mff have the same significance as mentioned above), or

a group of the formula:

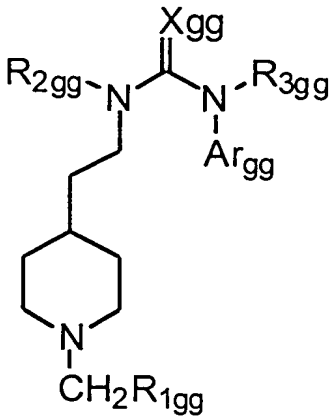


(wherein Xff has the same significance as mentioned above; Yff is hydrogen or a group of the formula: COR_{4ff} (where R_{4ff} is hydrogen or lower alkyl); pff is 2 or 3);

or salts thereof. Such compounds are exemplified by 1,4-dihydro-7-methoxy-4-methyl-1'-phenylmethylspiro[cyclopent-[b]indole-3(2H),4'-piperidine], 1,4-dihydro-4-methyl-1'-(4-methoxyphenyl)methylspiro[cyclopent[b]indole-3(2H),4'-piperidine], and the like.

The above-mentioned compounds or salts thereof may be produced according to the process as described in WO 97/37992 or its equivalent process.

8) Compounds of the formula:



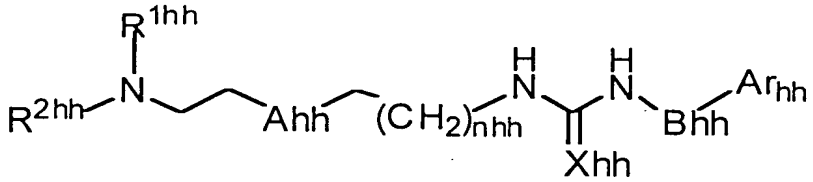
wherein R_{1gg} is C_{5-7} cycloalkyl, phenyl, or phenyl substituted by C_{1-4} alkyl, C_{1-4} alkoxy, nitro or halogen; R_{2gg} and R_{3gg} each is independently hydrogen or C_{1-4} alkyl; Xgg is

sulfur, oxygen, $CH-NO_2$ or $N-R_{5gg}$ (where R_{5gg} is hydrogen, hydroxy, C_{1-4} alkoxy, C_{1-4} alkyl, cyano or C_{1-4} alkylsulfonyl; Argg means a pyridyl or phenyl which may be substituted by 1 or more of substituents selected from halogen, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} acyl, cyano, nitro, trifluoromethyl and trifluoromethoxy;

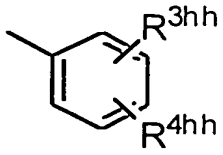
or salts thereof. Such compounds are exemplified by N-phenyl- N'-[2-(1-benzyl-4-piperidyl)ethyl]-1,1-diamino-2-nitro-ethylene, 1-(2-pyridyl)-3-[2-(1-benzyl-4-piperidyl)ethyl]-thiourea, 1-phenyl-2-hydroxy-3-[2-(1-benzyl-4-piperidyl)-ethyl]guanidine, and the like.

The above-mentioned compounds or salts thereof may be produced according to the process as described in JP-A 5-148228/1993 (EP-A 516520) or its equivalent process.

9) Compounds of the formula:

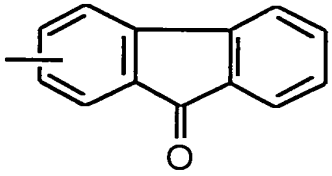


wherein R^{1hh} is C_{1-4} alkyl; R^{2hh} is C_{5-7} cycloalkyl, C_{5-7} cycloalkyl-methyl, benzyl, or benzyl substituted by C_{1-4} alkyl, C_{1-4} alkoxy, halogen or nitro; Ahh is oxygen or methylene; Bhh is a direct bonding, methylene or carbonyl; Arhh is pyridyl, a group of the following formula:

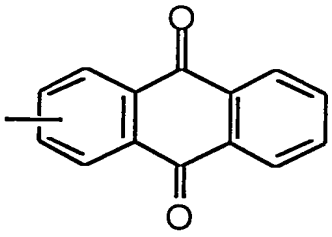


(wherein R^{3hh} and R^{4hh} each means independently hydrogen, halogen, nitro, C_{1-4} alkyl, C_{1-4} alkoxy, phenyl or trifluoromethoxy),

oxofluorenyl of the following formula:



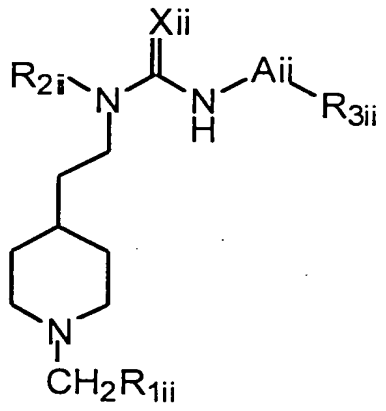
dioxoanthracenyl of the following formula:



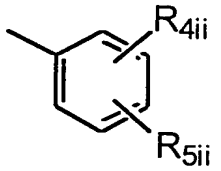
or naphthyl; nhh means 1 or 2; Xhh means oxygen or sulfur; or salts thereof. Such compounds are exemplified by 1-[2-[2-(N-benzyl-N-methylamino)ethoxy]ethyl]-3-(3-nitrobenzoyl)thiourea, 1-[2-[2-(N-benzyl-N-methylamino)ethoxy]ethyl]-3-(9-oxo-2-fluorenoyl)thiourea, and the like.

The above-mentioned compounds or salts thereof may be produced according to the process as described in JP-A 5-194359/1993 (EP-A 526313) or its equivalent process.

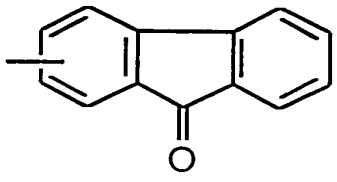
10) Compounds of the formula:



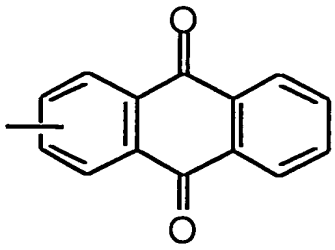
wherein R_{1ii} is C_{5-7} cycloalkyl, phenyl, or phenyl substituted by C_{1-4} alkyl, C_{1-4} alkoxy or halogen; R_{2ii} is hydrogen or C_{1-4} alkyl; Xii is oxygen or sulfur; Aii is methylene, carbonyl or sulfonyl; R_{3ii} is (1) a group of the formula:



(wherein R_{4ii} and R_{5ii} each is independently hydrogen, halogen, nitro, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} acyl, benzoyl, C_{1-4} alkylsulfonyl or trifluoromethoxy, or R_{4ii} and R_{5ii} taken together may form methylenedioxy); (2) a group of the formula:



or (3) a group of the formula:

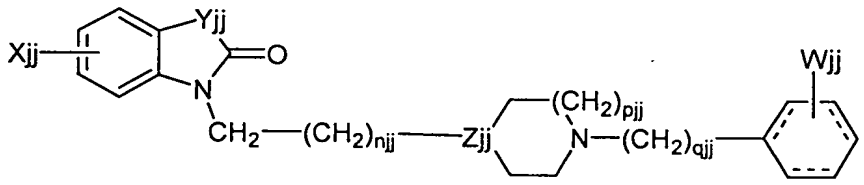


provided that when Xii is oxygen, Aii is a group other than methylene;

or salts thereof. Such compounds are exemplified by 1-(3-nitrobenzoyl)-3-[2-(1-benzyl-4-piperidyl)ethyl]thiourea, 1-(9,10-dioxo-2-anthracenoyl)-3-[2-(1-benzyl-4-piperidyl)-ethyl]thiourea, and the like.

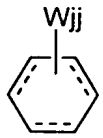
The above-mentioned compounds or salts thereof may be produced according to the process as described in PCT JP-A 6-507387/1994 (WO 92/14710) or its equivalent process.

11) Compounds of the formula:

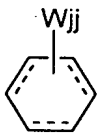


wherein njj is 1, 2 or 3; pjj is 1 or 2; qjj is 1 or 2; Xjj is independently a hydrogen atom, lower alkyl, aryl, aryloxy, CN, lower alkoxy, halogen, hydroxy, nitro, trifluoromethyl, alkylsulfonamido, NHCORjj (where Rjj is lower alkyl or aryl), $NR_{1jj}R_{2jj}$ (where R_{1jj} and R_{2jj} each is independently hydrogen or lower alkyl, or they taken together may form a ring), CO_2R_{jj} (where R_{jj} is lower alkyl),

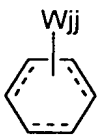
or in some cases one or more of substituents selected from further lower alkyl-substituted cycloalkyl, cycloalkenyl and bicycloalkyl; Yjj is CO or $CR_{3jj}R_{4jj}$ (where R_{3jj} and R_{4jj} each is independently a hydrogen atom, lower alkyl or lower alkoxy, or they taken together form a cyclic acetal); Zjj is N or CH; and the group of the formula:



is in some cases a substituted phenyl or cyclohexyl (where Wjj is independently one or more of substituents selected from hydrogen atom, lower alkyl, lower alkoxy and halogen); (provided that the following compounds are excluded: compounds in which njj=1, pjj=1, qjj=1, Xjj=H, Yjj=CO, Zjj=N, and the group of the formula:



is an unsubstituted phenyl; and compound in which njj=2, pjj=1, qjj=1, Xjj=H, Yjj=CO, Zjj=N, and the group of the formula:

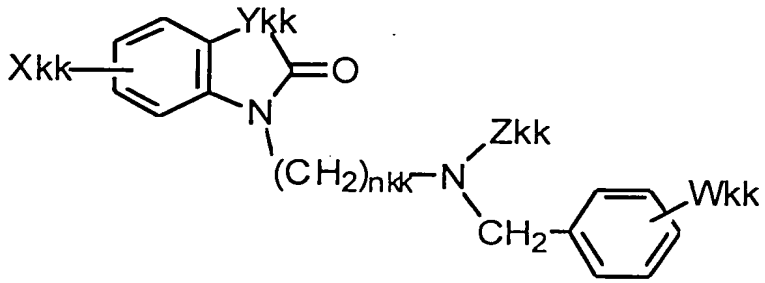


is 4-chlorophenyl);

or stereoisomers, optical isomers or racemates thereof, or their salts. Such compounds are exemplified by 5-cyclohexyl-1,3-dihydro-1-[2-[1-(phenylmethyl)-4-piperidinyl]ethyl]-2H-indol-2-one, and the like.

The above-mentioned compounds or salts thereof may be produced according to the process as described in PCT JP-A 7-502272/1995 (WO 93/12085) or its equivalent process.

12) Compounds of the formula:



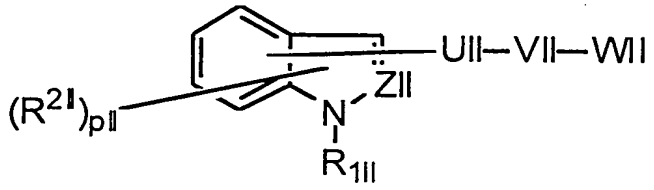
wherein nkk is 3, 4, 5, 6 or 7; Xkk is independently a hydrogen atom, lower alkyl, aryl, lower alkoxy, halogen, trifluoromethyl, nitro, $-NHCOR_{kk}$ (where R_{kk} is lower alkyl or aryl), $-NR_{1kk}R_{2kk}$ (where R_{1kk} and R_{2kk} each is independently hydrogen or lower alkyl, or they taken together form a ring), or in some cases one or more of substituents selected from further lower alkyl-substituted cycloalkyl, cycloalkenyl and bicycloalkyl; Ykk is CO or $CR_{3kk}R_{4kk}$ (where R_{3kk} and R_{4kk} each is independently a hydrogen atom, lower alkyl or lower alkoxy, or they taken together form a cyclic acetal); Zkk is lower alkyl; and Wkk is one or more of

substituents selected from hydrogen atom, lower alkyl, lower alkoxy and halogen;

or stereoisomers, optical isomers or racemates thereof, or their salts. Such compounds are exemplified by 5-cyclohexyl-1,3-dihydro-1-[5-(N-ethyl-N-phenylmethylamino)pentyl]-2H-indol-2-one, 5-cyclohexyl-1-[5-(N-ethyl-N-phenylmethylamino)-pentyl]-1H-indole-2,3-dione, and the like.

The above-mentioned compounds or salts thereof may be produced according to the process as described in PCT JP-A 8-511515/1996 (WO 94/29272) or its equivalent process.

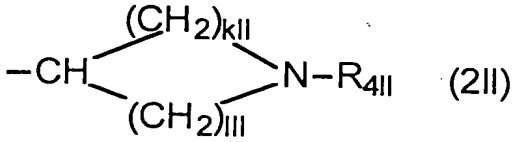
13) Compounds of the formula (III):



(III)

wherein R_{111} and R^{211} each is hydrogen, a group selected from the following substituent group All, or aryl, aralkyl, aralkyloxycarbonyl, arylamino, arylamino- alkyl, heterocyclic group, heterocyclic alkyl or heterocyclic aminoalkyl which may respectively be substituted by 1 to 3 (same or different) substituents selected from the following substituent group All; pll is an integer of 1 to 3; Ull is a group of the formula: -CO- or $-CH(OR_{311})-$ (where

R_{311} is hydrogen or hydroxy-protecting group); V11 is a group of the formula: -(CH=CH)m11- (CH_2)n11- (where m11 is an integer of 0 to 2; n11 is an integer of 0 to 7; provided that m11 and n11 are not 0 concurrently); W11 is a nitrogen-containing heterocyclic group which has an attaching point with V11 on the endocyclic nitrogen atom, a group of the formula (211):



(211)

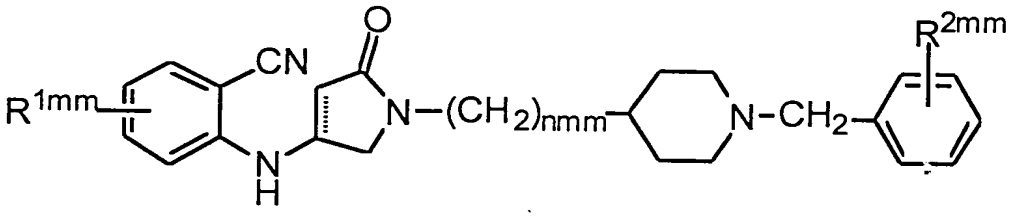
(wherein k11 and l11 are the same or different representing 1 to 4; R_{411} has the same significance as in R_{511} and R_{611} as mentioned below), or, in the above-mentioned general formula (211), when the cyclic alkylene forms 5- or 6-membered ring, a group in which said ethylene of the 5- or 6-membered ring is condensed with 1 or 2 benzene rings, or a group of the formula: $-NR_{511}R_{611}$ (where R_{511} and R_{611} each is hydrogen, a group selected from the following substituent group A11, or an aryl, arylcarbonyl, aralkyl, heterocyclic or heterocyclic alkyl which may be substituted by 1 to 3 substituents selected from the following substituent group A11);

The substituent group A11: Lower alkyl, cycloalkyl, aryl, heterocyclic group, aralkyl, halogen, amino, lower alkylamino, arylamino, amino lower alkyl, lower

alkylaminoalkyl, lower alkynylaminoalkyl, nitro, cyano, sulfonyl, lower alkylsulfonyl, halogenoalkylsulfonyl, lower alkanoyl, arylcarbonyl, arylalkanoyl, lower alkoxy, lower alkoxycarbonyl, halogeno-lower alkyl, N-lower alkynyl, N-cyanoamino, N-lower alkynyl and N-methylaminomethyl; or salts thereof. Such compounds are exemplified by 1-methyl- 3-[3-(1-benzyl-4-piperidyl)propionyl]indole, 1-methyl-3-[3-[1-(3-fluorobenzyl)-4-piperidyl]propionyl]-5-fluoroindole, 1-methyl-3-[3-[1-(2-chlorobenzyl)-4-piperidyl]propionyl]-indazole, and the like.

The above-mentioned compounds or salts thereof may be produced according to the process as described in JP-A 6-41070/1994 (EP-A 562832) or its equivalent process.

14) Compounds of the formula:



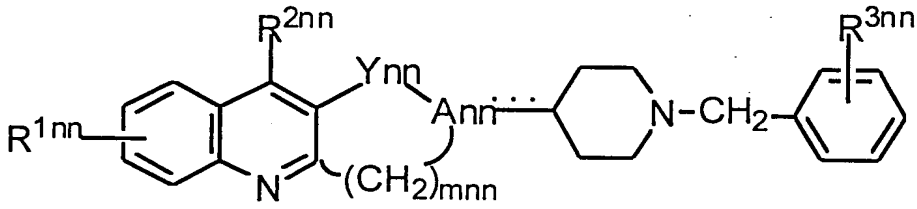
[wherein R^{1mm} is hydrogen, halogen, alkyl, alkoxy or alkylthio; R^{2mm} is hydrogen, halogen, alkyl or alkoxy; nmm is an integer of 0 - 7; the broken line indicates the optional presence of a double bond]

or salts thereof. Such compounds are exemplified by N-[1-[4-(1-benzylpiperidyl)ethyl]-2-oxo-3-pyrrolin-4-yl]-2-aminobenzonitrile, N-[1-[4-(1-benzylpiperidyl)propyl]-2-

oxo-3-pyrrolin-4-yl]-2-aminobenzonitrile, and the like.

The above-mentioned compounds or salts thereof may be produced according to the process as described in JP-A 5-9188/1993 or its equivalent process.

15) Compounds of the formula:



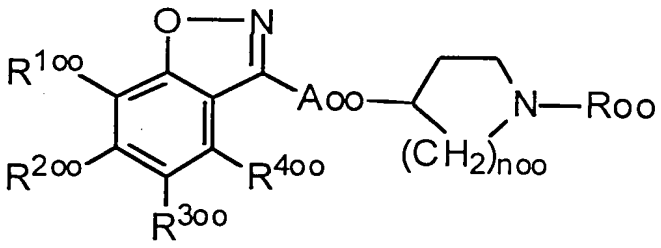
wherein >Ann··· represents >N-(CH_2)nnn-, >C=, >C=CH(CH_2)nnn- or >CH(CH_2)nnn- (where nnn is an integer of 0 - 7); Ynn is >C=O or >CHOH; R^{1nn} is hydrogen, halogen, alkyl, alkoxy or alkylthio; R^{2nn} is hydrogen, halogen, hydroxy, alkyl, alkoxy, optionally substituted phenyl, phenoxy, alkanoyl or optionally substituted amino; R^{3nn} is hydrogen, halogen, alkyl or alkoxy; mnn is an integer of 1 - 3;

or salts thereof. Such compounds are exemplified by 9-amino- 2-[4-(1-benzylpiperidyl)ethyl]-2,3-dihydropyrrolo[3,4-b]-quinolin-1-one, 9-amino-2-[2-(1-benzylpiperidin-4-yl)ethyl]- 1,2,3,4-tetrahydroacridin-1-one, 9-methoxy-2-[4-(1-benzyl-piperidyl)ethyl]-2,3-dihydropyrrolo[3,4-b]quinoline-1-one, and the like.

The above-mentioned compounds or salts thereof may be produced according to the process as described in

JP-A 5-279355/1993 (EP-A 481429) or its equivalent process.

16) Compounds of the formula:

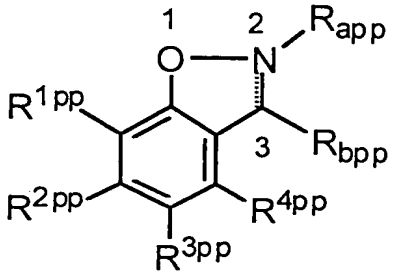


wherein R_{oo} is hydrogen, alkyl, alkenyl, cycloalkylalkyl, phenylalkyl, naphthylalkyl, cycloalkylalkenyl, phenylalkenyl or naphthylalkenyl; R^{1oo}, R^{2oo}, R^{3oo} and R^{4oo} are the same or different each representing hydrogen atom, halogen, alkyl, phenyl, phenyl- alkyl, alkoxy, heteroaryl, heteroarylalkyl, phenylalkoxy, phenoxy, heteroarylalkoxy, heteroaryloxy, acyl, acyloxy, hydroxy, nitro, cyano, -$NHCOR^{5oo}$, -$S(O)_{moo}R^{5oo}$, -$NHSO_2R^{5oo}$, -$CONR^{6oo}R^{7oo}$, -$NR^{6oo}R^{7oo}$, -$OCONR^{6oo}R^{7oo}$, -$OCSNR^{6oo}R^{7oo}$, -$SO_2NR^{6oo}R^{7oo}$ or -$COOR^{8oo}$; or R^{1oo}, R^{2oo}, R^{3oo} and R^{4oo} are taken together, when they are adjacent each other, to form an optionally substituted -$O(CH_2)$poo-, -$O(CH_2)$qooO-, -$O(CH_2)$rooN(R^{9oo})-, -$O(CH_2)$soo-CON(R^{9oo})-, -N(R^{9oo})CO-CH=CH- or a group forming benzene ring or heteroaromatic ring (where R^{5oo} is alkyl, phenyl or phenylalkyl; R^{6oo} and R^{7oo} are the same or different each representing a hydrogen atom, alkyl, phenyl or phenylalkyl, or they taken with the adjacent nitrogen atom may form a heterocycle; R^{8oo} is alkyl, phenyl or phenylalkyl; R^{9oo} is hydrogen, alkyl, phenylalkyl or acyl; moo is 0, 1 or 2; poo,

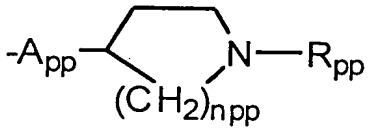
qoo, roo and soo are the same or different representing 1, 2 or 3); Aoo is a straight or branched chain alkylene; noo is 1, 2 or 3; in the above-mentioned definition, the alkyl, alkenyl, alkoxy, phenyl, phenoxy, cycloalkylalkyl, phenylalkyl, naphthylalkyl, cycloalkylalkenyl, phenylalkenyl, naphthylalkenyl, phenylalkoxy, heteroaryl, heteroaryloxy, heteroarylalkyl, heteroarylalkoxy, benzene ring and heteroaromatic ring may be substituted by 1 to 3 substituents selected from halogen, alkyl, alkoxy, acyl, acyloxy, hydroxy, nitro, cyano, $-NHCOR^{5oo}$, $-S(O)_{moo}R^{5oo}$, $-NHSO_2R^{5oo}$, $-CONR^{6oo}R^{7oo}$, $-NR^{6oo}R^{7oo}$, $-OCONR^{6oo}R^{7oo}$, $-OCSNR^{6oo}R^{7oo}$, $-SO_2NR^{6oo}R^{7oo}$ or $-COOR^{8oo}$; (where R^{5oo}, R^{6oo}, R^{7oo}, R^{8oo} and moo have the same significance as mentioned above); or salts thereof. Such compounds are exemplified by 3-[2-(1-benzyl-4-piperidyl)ethyl]-6,7-dimethoxy-1,2-benzisoxazole, 3-[2-(1-benzyl-4-piperidyl)ethyl]-6-(N-methyl-acetamino)-1,2-benzisoxazole, and the like.

The above-mentioned compounds or salts thereof may be produced according to the process as described in JP-A 5-320160/1993 (WO 93/04063) or its equivalent process.

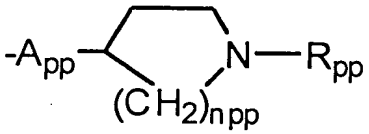
17) Compounds of the formula:



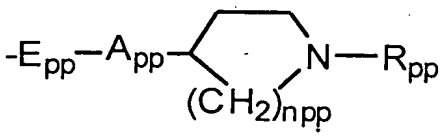
wherein when the bonding between the 2- and 3-positions is a single bond, R_{app} represents a group of the formula:



(wherein Rpp is hydrogen, alkyl, alkenyl, cycloalkyl- alkyl, cycloalkylalkenyl, phenylalkyl, phenylalkenyl, naphthylalkyl or naphthylalkenyl; App is straight or branched chain alkylene; npp is 1, 2 or 3), and R_{bpp} is oxygen; when the bonding between the 2- and 3-positions is a double bond, then R_{app} is absent, R_{bpp} represents a group of the formula:



(wherein each symbol has the same significance as mentioned above) or a group of the formula:



(wherein Epp is oxygen or sulfur, and the other symbols have the same significance as mentioned above); R^{1pp}, R^{2pp}, R^{3pp} and R^{4pp} are the same or different each representing hydrogen, halogen, alkyl, alkoxy, phenyl, phenylalkyl, phenylalkoxy, phenoxy, heteroaryl, heteroarylalkyl, heteroarylalkoxy, heteroaryloxy, acyl, acyloxy, hydroxy, nitro, cyano, $-NHCOR^{5pp}$, $-S(O)_{mpp}R^{5pp}$, $-NHSO_2R^{5pp}$, $-CONR^{6pp}R^{7pp}$, $-NR^{6pp}R^{7pp}$, $-OCSNR^{6pp}R^{7pp}$, $-SO_2NR^{6pp}R^{7pp}$ or $-COOR^{8pp}$ (where R^{5pp} is alkyl, phenyl or phenylalkyl; R^{6pp} and R^{7pp} are the same or different each representing hydrogen, alkyl, phenyl or phenylalkyl, or they taken together with the adjacent nitrogen atom form a heterocycle; R^{8pp} is hydrogen, alkyl, phenyl or phenylalkyl; mpp is 0, 1 or 2; in the above-mentioned definition, the alkyl, alkenyl, alkoxy, phenyl, phenylalkyl, phenylalkenyl, phenylalkoxy, phenoxy, cycloalkylalkyl, cycloalkylalkenyl, naphthylalkyl, naphthylalkenyl, heteroaryl, heteroarylalkyl, heteroarylalkoxy and heteroaryloxy may be substituted by 1 to 3 substituents selected from halogen, alkyl, alkoxy, acyl, acyloxy, hydroxy, nitro, cyano, $-NHCOR^{5pp}$, $-S(O)_{mpp}R^{5pp}$, $-NHSO_2R^{5pp}$, $-CONR^{6pp}R^{7pp}$, $-NR^{6pp}R^{7pp}$, $-OCONR^{6pp}R^{7pp}$, $-OCSNR^{6pp}R^{7pp}$, $-SO_2NR^{6pp}R^{7pp}$ or $-COOR^{8pp}$; (where R^{5pp}, R^{6pp}, R^{7pp}, R^{8pp} and mpp have the same significance as mentioned above);

or salts thereof. Such compounds are exemplified by 3-[2-(1-benzyl-4-piperidyl)ethyl]-6,7-dimethoxy-1,2-benzisox-

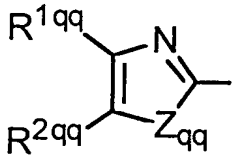
azole, 6-benzoylamino-2-[3-(1-benzyl-4-piperidyl)propyl]-1,2-benzisoxazol-3(2H)-one, 6-benzoylamino-2-[2-(1-benzyl-4-piperidyl)ethyl]-1,2-benzisoxazol-3(2H)-one, and the like.

The above-mentioned compounds or salts thereof may be produced according to the process as described in JP-A 6-41125/1994 (WO 93/04063) or its equivalent process.

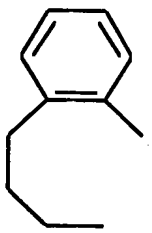
18) Compounds of the formula:

Mqq-Wqq-Yqq-Aqq-Qqq

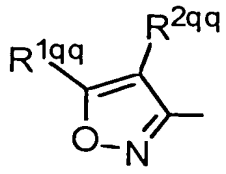
wherein Mqq is a group of formula:



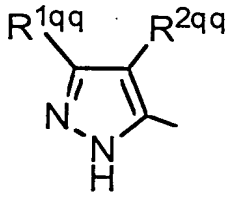
(wherein R^{1qq} is hydrogen, lower alkyl, optionally substituted heterocyclic group or optionally substituted aryl, and R^{2qq} is hydrogen, lower alkyl, optionally substituted heterocyclic group or optionally substituted aryl, or R^{1qq} and R^{2qq} taken each other form a group of the formula:



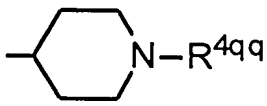
Zqq is S or O), a group of the formula:



(wherein R^{1qq} and R^{2qq} have the same significance as mentioned above), or a group of the formula:



(wherein R^{1qq} and R^{2qq} have the same significance as mentioned above); Wqq is a bonding, lower alkylene or lower alkenylene; Yqq is lower alkylene, -NH-, -CO-, a group of the formula: $-CONR^{3qq}-$ (where R^{3qq} is hydrogen or lower alkylene) or a group of the formula: $-CHR^{7qq}-$ (where R^{7qq} is hydroxy or protected hydroxy); Aqq is a bonding or lower alkylene; Qqq is a group of the formula: $-NR^{8qq}R^{9qq}$ (where R^{8qq} is lower alkyl; R^{9qq} is ar(lower)alkyl) or a group of the formula:



(wherein R^{4qq} is lower alkyl or optionally substituted ar(lower)alkyl);

or salts thereof. Such compounds are exemplified by 4-(pyridin-3-yl)-5-methyl-2-[[2-(1-benzylpiperidin-4-yl)-ethyl]carbamoyl]thiazole, 2-[[2-(1-benzylpiperidin-4-

yl)ethyl]carbamoyl]-4-(4-chlorophenyl)-5-methyloxazole, 5-[[2-(1-benzylpiperidin-4-yl)ethyl]carbamoyl]-3-(4-nitrophenyl)pyrazole, and the like.

The above-mentioned compounds or salts thereof may be produced according to the process as described in JP-A 5-345772/1993 or its equivalent process.

19) Compounds of the formula:

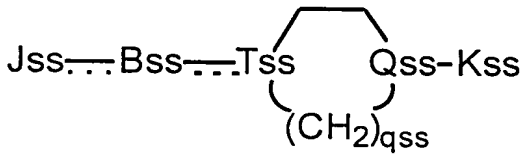
R_{1rr}-Qrr-Zrr-Xrr-Arr-Mrr

wherein R_{1rr} is lower alkyl, optionally substituted heterocyclic group, optionally substituted aryl, optionally substituted ar(lower)alkyl or ar(lower)alkenyl; Qrr is oxadiazolediyl; Zrr is a bonding or vinyl; Xrr is a bonding, a group of the formula: $-CONR_{4rr}-$ (where R_{4rr} is hydrogen or lower alkyl), a group of the formula: $-CHR_{8rr}-$ (where R_{8rr} is hydroxy or protected hydroxy), -CO- or -NHCO-; Arr is a bonding, lower alkylene or lower alkenylene; Mrr is a heterocyclic group which may be substituted by a substituent selected from lower alkyl, imino-protecting group and optionally substituted ar(lower)alkyl and which contains at least one nitrogen atom;

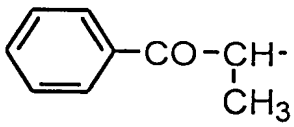
or salts thereof. Such compounds are exemplified by 5-(quinuclidin-3-yl)-3-[[2-(1-benzylpiperidin-4-yl)ethyl]-carbamoyl]-1,2,4-oxadiazole, 3-[[2-(1-benzylpiperidin-4-yl)ethyl]carbamoyl]-5-(4-nitrophenyl)-1,2,4-oxadiazole, and the like.

The above-mentioned compounds or salts thereof may be produced according to the process as described in PCT JP-A 7-502529/1995 (WO 93/13083) or its equivalent process.

20) Compounds of the formula:



[wherein Jss is (a) the following substituted or unsubstituted group: (1) phenyl, (2) pyridyl, (3) pyrazyl, (4) quinolyl, (5) cyclohexyl, (6) quinoxalyl, or (7) furyl, (b) a monovalent or divalent group selected from the following group, of which the phenyl moiety may be substituted: (1) indanyl, (2) indanonyl, (3) indenyl, (4) indenonyl, (5) indanedionyl, (6) tetralonyl, (7) benzsuberonyl, (8) indanolyl, or (9) a group of the formula:



(c) a monovalent group derived from a cyclic amide compound,

(d) lower alkyl, or

(e) a group of the formula R_{1ss}-CH=CH- (where R_{1ss} is hydrogen or lower alkoxycarbonyl);

Bss is a group of the formula: -(CHR_{2ss})nss-, a group of the

formula: -CO-(CHR_{2ss})nss-, a group of the formula: -NR_{3ss}-(CHR_{2ss})nss- (where R_{3ss} is hydrogen, lower alkyl, acyl, lower alkylsulfonyl, optionally substituted phenyl or benzyl), a group of the formula: -CO-NR_{4ss}-(CHR_{2ss})nss- (where R_{4ss} is hydrogen, lower alkyl or phenyl), a group of the formula: -CH=CH-(CHR_{2ss})nss-, a group of the formula: -O-COO-(CHR_{2ss})nss-, a group of the formula: -O-CO-NH-(CHR_{2ss})nss-, a group of the formula: -NH-CO-(CHR_{2ss})nss-, a group of the formula: -CH_2-CO-NH-(CHR_{2ss})nss-, a group of the formula: -$(CH_2)_2$-CO-NH-(CHR_{2ss})nss-, a group of the formula: -C(OH)H-(CHR_{2ss})nss- (in the above formulae, nss indicates 0 or an integer of 1 - 10; R_{2ss} means hydrogen or methyl when the alkylene of the formula -(CHR_{2ss})nss- has no substituent or it has 1 or more of methyl), a group of the formula: =(CH-CH=CH)bss- (where bss is an integer of 1 - 3), a group of the formula: =CH-(CH_2)css- (where css is 0 or an integer of 1 - 9), a group of the formula: =(CH-CH)dss= (where dss is 0 or an integer of 1 - 5), a group of the formula: -CO-CH=CH- CH_2-, a group of the formula: -CO-CH_2-C(OH)H-CH_2-, a group of the formula: -C(CH_3)H-CO-NH-CH_2-, a group of the formula: -CH=CH- CO-NH-$(CH_2)_2$-, a group of the formula: -NH-, a group of the formula: -O-, a group of the formula: -S-, dialkylaminoalkyl- carbonyl group or lower alkoxycarbonyl;

Tss is nitrogen or carbon atom;

Qss is nitrogen, carbon or a group of the formula >N→O;

Kss is hydrogen, substituted or unsubstituted phenyl, arylalkyl of which the phenyl moiety may be substituted, cinnamyl of which the phenyl moiety may be substituted, lower alkyl, pyridylmethyl, cycloalkylalkyl, admantanemethyl, furylmethyl, cycloalkyl, lower alkoxycarbonyl or acyl;

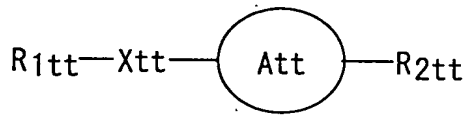
qss is an integer of 1 - 3;

$\equiv$ indicates a single bond or double bond;

or salts thereof. Such compounds are exemplified by 1-benzyl- 4-[(5,6-dimethoxy-1-indanon)-2-yl]methylpiperidine, N-[4'-(1'-benzylpiperidyl)ethyl]-2-quinoxalinecarboxylic amide, 4-[4'-(N-benzyl)piperidyl]-p-methoxybutyrophenone, 1-[4'-(1'-benzylpiperidin)ethyl]-1,2,3,4-tetrahydro-5H-1-benzazepin-2-one, and the like.

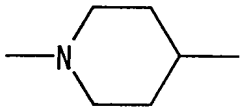
The above-mentioned compounds or salts thereof may be produced according to the process as described in JP-A 64-79151/1989 (USP 4,895,841) or its equivalent process.

21) Compounds of the formula:

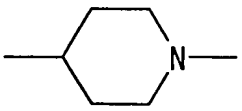


wherein R_{1tt} is a mono-valent group derived from a compound selected from optionally substituted benzene, pyridine, pyrazine, indole, anthraquinone, quinoline, optionally

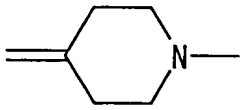
substituted phthalimide, homophthalimide, pyridinecarboxylic imide, pyridine-N-oxide, pyrazinecarboxylic imide, naphthalenedicarboxylic imide, optionally substituted quinazolidinedione, 1,8-naphthalimide, bicyclo[2.2.2]oct-5-ene-2,3-dicarboxylic imide and pyromellic imide; Xtt is a group of the formula: $-(CH_2)$mtt- (where mtt is an integer of 0 - 7), a group of the formula: $-O(CH_2)$ntt-, a group of the formula: $-S(CH_2)$ntt-, a group of the formula: $-NH(CH_2)$ntt-, a group of the formula: $-SO_2NH(CH_2)$ntt-, a group of the formula: $-NHCO(CH_2)$ntt-, a group of the formula: $-NH(CH_2)$ntt-CO-, a group of the formula: $-COO(CH_2)$ntt-, a group of the formula: $-CH_2NH(CH_2)$ntt-, a group of $-CONR_{3tt}-(CH_2)$ntt- (in the definition of Xtt, all of ntt in the formulae indicate an integer of 1 - 7; R_{3tt} is lower alkyl or benzyl group), a group of the formula: $-O-CH_2CH_2CH(CH_3)-$, a group of the formula: $-O-CH(CH_3)CH_2CH_2-$, a group of the formula: $-O-CH_2CH_2CH=$, a group of the formula: $-O-CH_2CH(OH)CH_2-$; the ring Att represents a group of the formula:



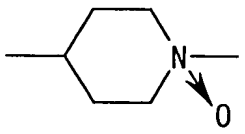
a group of the formula:



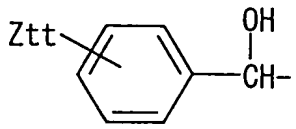
a group of the formula:



a group of the formula:



R_{2tt} is hydrogen, lower alkyl, optionally substituted benzyl, optionally substituted benzoyl, pyridyl, 2-hydroxyethyl, pyridylmethyl, or a group of the formula:



(wherein Ztt means halogen);

or salts thereof. Such compounds are exemplified by N-methyl- N-[2-(1'-benzylpiperidin-4'-yl)ethyl]-4-benzylsulfonylbenz-amide, N-[2-(N'-benzylpiperidin-4'-yl)ethyl]-4-nitrophthal-imide, N-[2-(N'-benzylpiperidin-4'-yl)ethyl]-1,8-naphthal-imide, and the like.

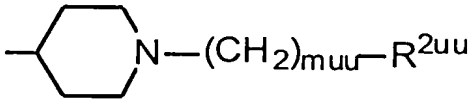
The above-mentioned compounds or salts thereof may be produced according to the process as described in JP-A 62-234065/1987 (EP-A 229391) or its equivalent process.

22) Compounds of the formula:

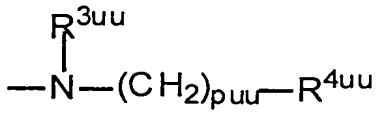
$R^{1uu}-(CH_2)nuu-Zuu$

wherein R^{1uu} is an optionally substituted group derived from cyclic amide compounds; nuu is 0 or an integer of 1 - 10;

Zuu is (1) a group of the formula:



(wherein R^{2uu} is optionally substituted aryl, cycloalkyl or heterocyclic group; muu is an integer of 1 - 6) or (2) a group of the formula:



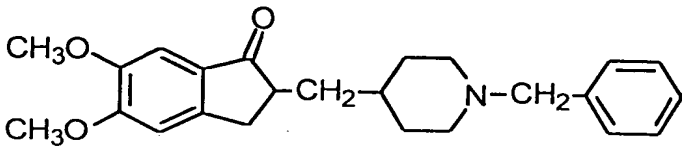
(wherein R^{3uu} is hydrogen or lower alkyl; R^{4uu} is optionally substituted aryl, cycloalkyl or heterocyclic group; puu is an integer of 1 - 6); provided that the following cases are excluded: when the optionally substituted cyclic amide compound is quinazolidinone or quinazolidinedione in the definition of R^{1uu}, and when R^{2uu} and R^{4uu} are aryl in the definition of Zuu;

or salts thereof. Such compounds are exemplified by 3-[2-(1-benzyl-4-piperidyl)ethyl]-5-methoxy-2H-3,4-dihydro-1,3-benzoxazin-2-one, 3-[2-[1-(4-pyridylmethyl)-4-piperidyl]-ethyl]-2H-3,4-dihydro-1,3-benzoxazin-2-one, 3-[2-[1-(1,3-dioxolan-2-ylmethyl)-4-piperidyl]ethyl]-5-methoxy-1,2,3,4-tetrahydroquinazoline-2,4-dione, 3-[2-(1-benzyl-4-piperidyl)ethyl]-6-methoxy-2H-3,4-dihydro-1,3-benzoxadine-2,4-dione, and the like.

The above-mentioned compounds or salts thereof may be produced according to the process as described in

JP-A 4-235161/1992 (EP-A 468187) or its equivalent process.

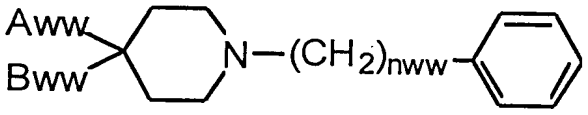
23) An optically active indanone derivatives deriof the formula:



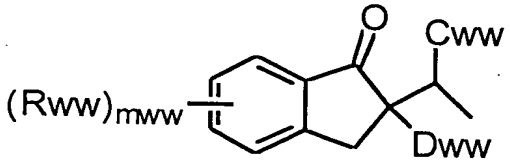
or salts thereof.

The above-mentioned compound or salts thereof may be produced according to the process as described in JP-A 4-21670/1992 or its equivalent process.

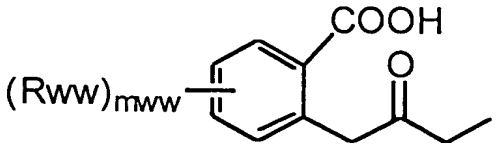
24) Compounds of the formula:



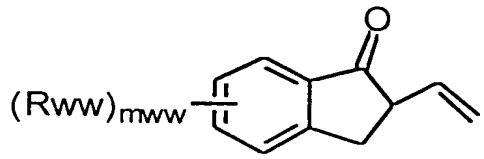
[wherein nww is 0 or an integer of 1 or 2; Aww is a group of the formula:



(wherein Cww is hydrogen or hydroxy; Dww is hydrogen or lower hydroxyalkyl; Rww is the same or different representing a group selected from hydrogen atom, lower alkyl and lower alkoxy; mww is 0 or an integer of 1 - 4) or a group of the formula:



(wherein each symbol has the same significance as mentioned above); Bww is hydrogen or hydroxy; or alternatevly, Aww and Bww taken together form a double bond to form a group of the formula:

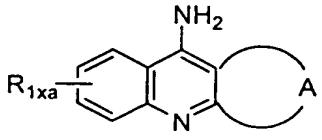


(wherein each symbol has the same significance as mentioned above);

or salts thereof. Such compounds are exemplified by 1-benzyl-4- (5,6-dimethoxy-1-indanon-2-yl)hydroxymethylpiperidine, 1-benzyl-4-(5,6-dimethoxy-2-hydroxymethyl-1-indanon-2-yl)-methylpiperidine, 1-benzyl-4-[3-(4,5-dimethoxy-2-carboxy-phenyl)-2-oxo]propylpiperidine, and the like.

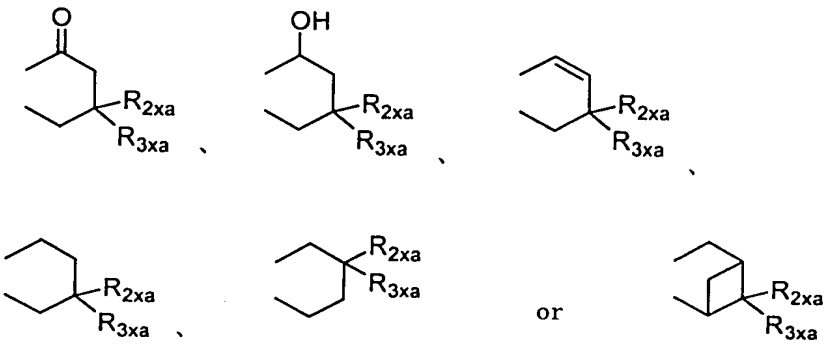
The above-mentioned compounds or salts thereof may be produced according to the process as described in JP-A 9-268176/1997 or its equivalent process.

25) Compounds of the formula:



wherein R_{1xa} is hydrogen, halogen, hydroxy, lower alkoxy, lower alkyl or mono(or di or tri)halo(lower)alkyl; the group of the formula:

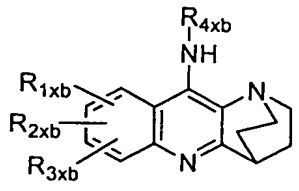
represents a moiety of the formula:



(wherein R_{2xa} and R_{3xa} each is lower alkyl);
or salts thereof. Such compounds are exemplified by 9-amino-6-chloro-3,3-dimethyl-1,2,3,4-tetrahydroacridine, and the like.

The above-mentioned compounds or salts thereof may be produced according to the process as described in JP-A 2-167267/1990 or its equivalent process.

26) Aminoazaacridine derivatives of the formula:

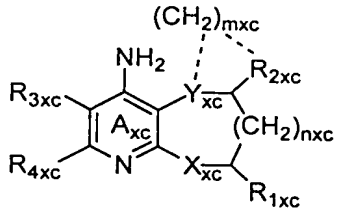


wherein R_{1xb}, R_{2xb} and R_{3xb} each is hydrogen, halogen, trifluoromethyl, lower alkyl, lower cycloalkyl, lower

alkoxy, lower alkoxymethyl, lower alkylthio, nitro, amino, lower alkanoylamino, lower alkylamino, hydroxy, phenyl or phenyl substituted by halogen, lower alkyl or lower alkoxy; R_{4xb} is hydrogen, lower alkyl, aralkyl, diaralkyl, or a group of the formula: R_{5xb}-CO- (R_{5xb} is lower alkyl, lower cycloalkyl, aralkyl, phenyl or phenyl substituted by halogen, lower alkyl or lower alkoxy);
or salts thereof. Such compounds are exemplified by 9-amino- 8-fluoro-1,2,3,4-tetrahydro-1,4-ethano-1-azaacridine, and the like.

The above-mentioned compounds or salts thereof may be produced according to the process as described in JP-A 63-166881/1988 or its equivalent process.

27) Compounds of the formula:

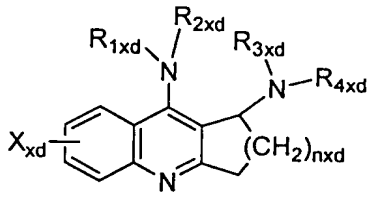


wherein R_{1xc} is hydrogen or lower alkyl; R_{2xc} is independently hydrogen or lower alkyl, or it taken with R_{6xc} forms a cyclic alkylene chain; R_{3xc} and R_{4xc} each is independently hydrogen, or they taken together with the ring A_{xc} form a quinoline ring or tetrahydroquinoline ring; X_{xc} is oxygen, sulfur or N-R_{5xc}, and R_{5xc} is hydrogen or lower alkyl; Y_{xc} is oxygen or N-R_{6xc}, and R_{6xc} is independently

hydrogen or lower alkyl, or it taken with R_{2xc} forms a cyclic alkylene; nxc is 0 or 1; mxc is an integer of 0 - 4; or salts thereof. Such compounds are exemplified by 4'-amino- quinolino[2,3-b]-4-methyl-5,6-dihydro-1,4-oxazine, 4'-amino- 5',6',7',8'-tetrahydroquinolino[2,3-b]-4-methyl-5,6-dihydro-1,4-oxazine, and the like.

The above-mentioned compounds or salts thereof may be produced according to the process as described in JP-A 2-96580/1990 or its equivalent process.

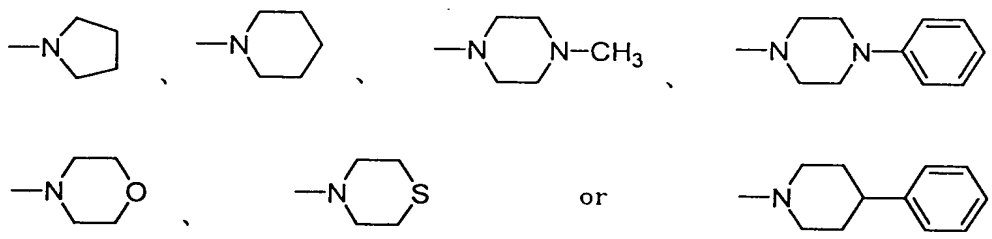
28) Compounds of the formula:



wherein nxd is 1, 2 or 3, and Xxd is hydrogen, lower alkyl, lower alkoxy, halogen, hydroxy, nitro or trifluoromethyl;

R_{1xd} and R_{2xd} each is independently hydrogen, lower alkyl or aryl lower alkyl, but they cannot be aryl lower alkyl concurrently;

R_{3xd} and R_{4xd} each is independently hydrogen, lower alkyl, aryl lower alkyl, formyl or lower alkylcarbonyl, or the group $-NR_{3xd}R_{4xd}$ represents the following group:

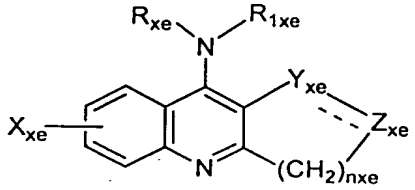


as a whole;

or stereoisomers thereof or their salts. Such compounds are exemplified by 1-(1-piperidinyl)-1,2,3,4-tetrahydro-9-acridinamine, N-1-ethyl-1,2,3,4-tetrahydro-1,9-acridine-diamine, and the like.

The above-mentioned compounds or salts thereof may be produced according to the process as described in JP-A 3-153667/1991 or its equivalent process.

29) Compounds of the formula:



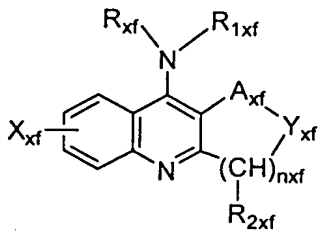
wherein nxe is 1, 2 or 3; X_{xe} is hydrogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, hydroxy, nitro, trifluoromethyl, $NHCOR_{2xc}$ (where R_{2xc} is C_1-C_6 alkyl) or $NR_{3xc}R_{4xc}$ (where R_{3xc} and R_{4xc} are independently hydrogen or C_1-C_6 alkyl); R_{xc} is hydrogen or C_1-C_6 alkyl; R_{1xc} is hydrogen, C_1-C_6 alkyl, di-C_1-C_6 alkylamino-C_1-C_6 alkyl, aryl-C_1-C_6 alkyl, diaryl-C_1-C_6 alkyl, furyl-C_1-C_6 alkyl, thienyl-C_1-C_6 alkyl, oxygen-bridged aryl-C_1-C_6 alkyl, oxygen-bridged diaryl-C_1-C_6 alkyl, oxygen-bridged furyl-C_1-C_6 alkyl, or oxygen-bridged thienyl-C_1-C_6 alkyl; Y_{xe} is C=O or $CR_{5xc}OH$ (where R_{5xc} is hydrogen or C_1-C_6 alkyl); and Z_{xe} is CH_2 or $C=CR_{6xc}R_{7xc}$ (where R_{6xc} and R_{7xc} are independently hydrogen or C_1-C_6 alkyl), or Y_{xe} and Z_{xe} taken together form CR_{5xc}=CH (where CR_{5xc} and CH respectively

correspond to Y_{xe} and Z_{xe});

or optical antipodes thereof or their salts. Such compounds are exemplified by 9-amino-3,4-dihydroacridin-1(2H)-one, 9-amino- 1,2,3,4-tetrahydroacridin-1-ol, and the like.

The above-mentioned compounds or salts thereof may be produced according to the process as described in JP-A 61-148154/1986 or JP-B 5-41141/1993 or its equivalent process.

30) Compounds of the formula:



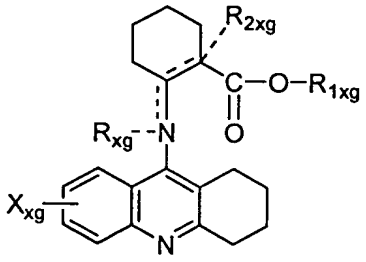
wherein nxf is 1 - 4; R_{xf} is hydrogen, lower alkyl or lower alkylcarbonyl; R_{1xf} is hydrogen, lower alkyl, lower alkyl-carbonyl, aryl, di(lower)alkylamino(lower)alkyl, aryl lower alkyl, diaryl lower alkyl, oxygen-bridged aryl lower alkyl, or oxygen-bridged diaryl lower alkyl; Axf is a direct bonding or (CHR_{3xf})mxf; mxf is 1 - 3; Xxf is hydrogen, lower alkyl, cyclo- alkyl, lower alkoxy, halogen, hydroxy, nitro, trifluoromethyl, formyl, lower alkylcarbonyl, arylcarbonyl, -SH, lower alkyl- thio, $-NHCOR_{4xf}$ or $NR_{5xf}R_{6xf}$; in the above formulae, R_{4xf} is hydrogen or lower alkyl; R_{5xf} and R_{6xf} each is independently hydrogen, lower alkyl or cycloalkyl; Yxf

is O, S or NR_{7xf}; each R_{2xf}, each R_{3xf} and R_{7xf} are independently hydrogen or lower alkyl, or two of them concurrently form a methylene or ethylene group which constitutes a moiety of a ring comprising at least 5 atoms; provided that when Axf is CH_2, Yxf is NCH_3, (CHR_{2xf})nxf is CH_2CH_2, Xxf is H, CH_3, Cl, Br or NO_2, and R_{xf} is H, then R_{1xf} is neither H, methyl, ethyl, propyl, butyl nor benzyl; when Axf is $-CH_2-$ or CHR'-, Yxf is NH or NR', and (CHR_{2xf})nxf is $-CH_2CH_2-$ or $CH_2CHR'-$, then the group $-NR_{xf}R_{1xf}$ is neither $-NH_2$, $-NHC_6H_5$ nor di(lower) alkylamino(lower)alkylamino, and each R' is independently lower alkyl; when Axf is CH_2, Yxf is NH or NR', and (CHR_{2xf})nxf is $-(CH_2)_3-$ or $CHR'CH_2CH_2-$, then the group $-NR_{xf}R_{1xf}$ is not $-NH_2$; when Axf is $-CH_2CH_2-$, Yxf is NH or NR', and (CHR_{2xf})nxf is $-CH_2CH_2-$ or $CHR'CH_2-$, then the group $-NR_{xf}R_{1xf}$ is not $-NH_2$;

or optical or geometrical isomers thereof or their salts. Such compounds are exemplified by 9-amino-2,3-dihydrothieno[3,2-b]quinoline, 10-amino-3,4-dihydro-1H-thiopyrano[4,3-b]-quinoline, and the like.

The above-mentioned compounds or salts thereof may be produced according to the process as described in JP-A 63-284175/1988 or its equivalent process.

31) Compounds of the formula:

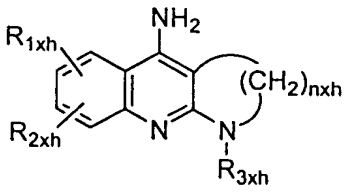


wherein Xxg is hydrogen, lower alkyl, lower alkoxy or halogen; R_{xg} is, when it is present, hydrogen, lower alkyl or aryl lower alkyl; R_{1xg} is hydrogen, lower alkyl or aryl lower alkyl; and R_{2xg} is, when it is present, hydrogen or lower alkyl;

or salts thereof. Such compounds are exemplified by 2-(1,2,3,4- tetrahydro-9-acridinimino)cyclohexanecarboxylic acid, ethyl 2-(1,2,3,4-tetrahydro-9-acridinimino)cyclohexanecarboxylate, and the like.

The above-mentioned compounds or salts thereof may be produced according to the process as described in JP-A 3-95161/1991 or its equivalent process.

32) Compounds of the formula:



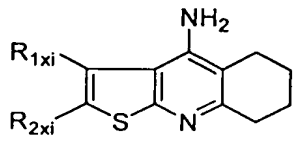
wherein R_{1xh} and R_{2xh} each is hydrogen, halogen, lower alkyl, trifluoromethyl, hydroxy, lower alkoxy, lower alkanoyloxy, nitro, amino or lower alkanoylamino; R_{3xh} is hydrogen, alkyl of 1 - 15 carbon atoms, cycloalkyl, aralkyl of 7 - 15 carbon atoms optionally substituted by halogen, lower alkyl

or lower alkoxy, alkanoyl of 2 - 15 carbon atoms, or benzoyl which may be substituted by halogen, lower alkyl, lower alkoxy, nitro, hydroxy or amino; nxh is an integer of 2 - 5;

or salts thereof. Such compounds are exemplified by 6-amino-1- benzyl-2,3,4,5-tetrahydro-1H-azepino[2,3-b]quinoline, 5-amino-6-fluoro-1,2,3,4-tetrahydrobenzo[d][1,8]naphthyridine, and the like.

The above-mentioned compounds or salts thereof may be produced according to the process as described in JP-A 3-220189/1991 or its equivalent process.

33) 4-Amino-5,6,7,8-tetrahydrothieno[2,3-b]quinoline derivatives of the formula:

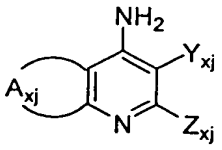


wherein R_{1xi} and R_{2xi} each is hydrogen or straight or branched chain alkyl of 1 - 4 carbon atoms, provided that they are not hydrogen concurrently;

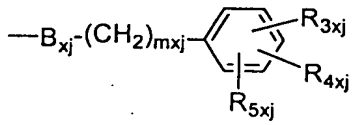
or salts thereof. Such compounds are exemplified by 4-amino- 2,3-dimethyl-5,6,7,8-tetrahydrothieno[2,3-b]quinoline, and the like.

The above-mentioned compounds or salts thereof may be produced according to the process as described in JP-A 4-134083/1992 or its equivalent process.

34) 4-Amino-2,3-cycloalkenopyridine and 4-aminoquinoline derivatives of the formula:

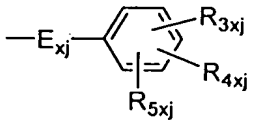


wherein Axj represents alkylene of the formula $-(CH_2)nxj-$ (where nxj is an integer of 3 - 5), which is bound to two adjacent carbon atoms on the adjacent pyridine nucleus to form a cycloalkenone group or which is associated with two adjacent carbon atoms on the adjacent pyridine nucleus to form a benzene ring; and (i) when Axj forms a cycloalkenone group, then Yxj represents hydrogen, halogen, C1-C6 lower alkyl or amino, and Zxj represents hydrogen, hydroxy, halogen, amino, a group of the formula $-NR_{1xj}R_{2xj}$ (R_{1xj} and R_{2xj} are the same or different representing lower alkyl or benzyl), pyrrolidyl, piperidyl, piperazyl, N-substituted piperazyl, pyridyl, or a group of the formula:



(wherein B is oxygen or sulfur; mxj is an integer of 0 - 2; R_{3xj}, R_{4xj} and R_{5xj} are the same or different representing hydrogen, halogen, trifluoromethyl, hydroxy, lower alkoxy, straight or branched (C_1-C_6) lower alkyl, amino, or acylamino), or Zxj represents pyridylthio; and (ii) when Axj forms a benzene ring, then Yxj represents hydrogen or

C_1-C_6 lower alkyl, and Zxj represents a group of the formula $-CONR_{6xj}R_{7xj}$ (where R_{6xj} and R_{7xj} each is hydrogen or C_1-C_6 lower alkyl, or alternatively R_{6xj} and R_{7xj} are taken together to form a C_3-C_6 cycloalkyl), or Zxj represents a group of the formula:

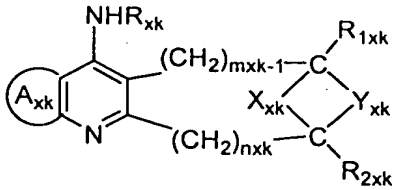


wherein Exj is C_2-C_6 alkylene or a group of the formula -(CH=CH)pxj- (where pxj is 1 or 2), and R_{3xj}, R_{4xj} and R_{5xj} have the same significance as mentioned above;

or salts thereof. Such compounds are exemplified by 4-amino- 2-(N-methylcarbamoyl)quinoline, and the like.

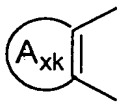
The above-mentioned compounds or salts thereof may be produced according to the process as described in JP-A 4-66571/1992 or its equivalent process.

35) Polycyclic aminopyridine compounds of the formula:

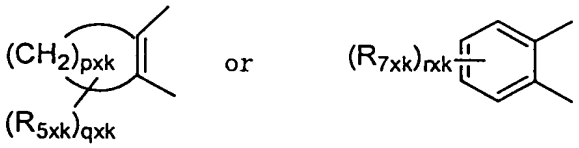


wherein R_{xk} is hydrogen, alkyl, aralkyl or acyl; R_{1xk} and R_{2xk} each is independently hydrogen, alkyl, aralkyl, alkoxy, alkoxy-carbonyl, amino or amino substituted by 1 or 2 of alkyl, aralkyl or acyl; mxk and nxk each is 1, 2 or 3; Xxk and Yxk each is independently a bonding between two carbon

atoms, oxygen or sulfur, a group N-R_{3xk} (where the group R_{3xk} and R_{xk} have the same significance as mentioned above), or an alkylene or alkenylene crosslink which contains 1 - 5 carbon atoms and may contain 1 or more of the substituent R_{4xk} (where R_{4xk} is independently hydrogen, straight or branched chain lower alkyl of 1 - 4 carbon atoms, alkenyl or alkylidene, phenyl or phenyl which is substituted by 1 or more of lower alkyl of 1 - 4 carbon atoms, lower alkoxy of 1 - 4 carbon atoms or halogen, aralkyl, lower alkoxy of 1 - 4 carbon atoms, or hydroxy); and when Yxk is alkenylene, the latter can be condensed with a saturated or unsaturated carbocyclic or heterocyclic ring, and the above-mentioned ring may be substituted by 1 or more of groups of R_{5xk} (R_{5xk} is hydrogen, lower alkyl or lower alkoxy of 1 - 4 carbon atoms, or halogen); and the group of formula:



represents a moiety of the formula:



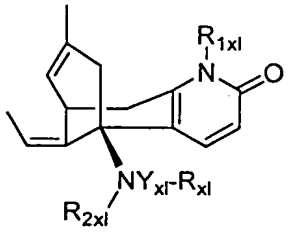
;pxk, qxk and rxk each is 1 or more; and R_{6xk} or R_{7xk} may be independently hydrogen, halogen, lower alkoxy or lower alkyl;

or salts thereof. Such compounds are exemplified by (+)-

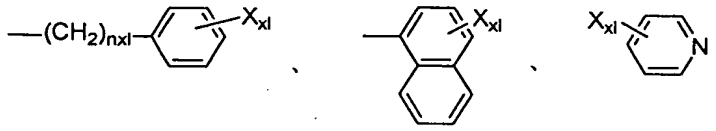
12-amino-6,7,10,11-tetrahydro-9-ethyl-7,11-methanocycloocta-[b]quinoline, (+)-12-amino-6,7,10,11-tetrahydro-9-methyl-7,11-methanocycloocta[b]quinoline, and the like.

The above-mentioned compounds or salts thereof may be produced according to the process as described in PCT JP-A 11-500144/1999 or its equivalent process.

36) Compounds of the formula:



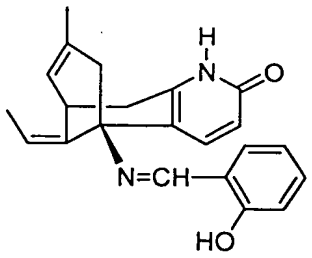
wherein Y_{xl} is -C=O or $-R_{2xl}$; Y is =CH; R_{xl} is C_1-C_5 lower alkyl, a group of the formulae:



(where nxl = 0 or 1; Xxl is hydrogen, C_1-C_5 lower alkyl, C_1-C_5 lower alkoxy, nitro, halogen, carboxy, alkoxycarbonyl, hydroxymethyl, hydroxy, bis-C_1-C_5 lower alkyl-substituted amino), $-(CH_2)_{mxl}COOZxl$ (where mxl = 0 - 5; Zxl is hydrogen or C_1-C_5 lower alkyl), -CH=CH-Gxl (where Gxl is phenyl, furanyl, carboxy, or alkoxycarbonyl), and dihydro- or tetrahydro-pyridyl substituted by C_1-C_5 lower alkyl at the nitrogen atom; R_{1xl} is hydrogen, C_1-C_5 lower alkyl, pyridoyl

and C_1-C_5 lower alkoxy-substituted benzoyl; R_{2x1} is hydrogen or C_1-C_5 lower alkyl;

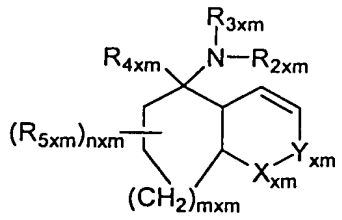
or salts thereof. Such compounds are exemplified by one of the formula:



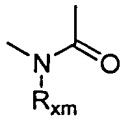
and the like.

The above-mentioned compounds or salts thereof may be produced according to the process as described in PCT JP-A 10-511651/1998 or its equivalent process.

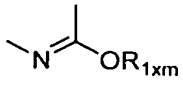
37) Compounds of the formula:



wherein Xxm-Yxm is a group of the formula:

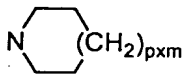


(wherein R_{xm} is hydrogen, lower alkyl, lower alkenyl, lower alkynyl or aryl lower alkyl) or a group of the formula:

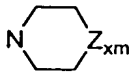


(wherein R_{1xm} is hydrogen, lower alkyl or aryl lower alkyl);

R_{2xm} and R_{3xm} each is independently hydrogen, lower alkyl, aryl lower alkyl, diaryl lower alkyl, lower cycloalkenyl lower alkyl, lower alkoxy, aryl lower alkoxy or lower alkanoyl, or R_{2xm} and R_{3xm} taken with the attached nitrogen atom form a group of the formula:



(wherein pxm is 0 or 1) or a group of the formula:

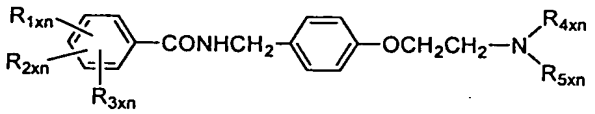


(wherein Zxm is O, S or a group of the formula NR_{6xm} (R_{6xm} is hydrogen, lower alkyl or aryl lower alkyl)); R_{4xm} is hydrogen, lower alkyl or aryl lower alkyl; R_{5xm} is hydrogen, lower alkyl or aryl lower alkyl; mxm is 0, 1 or 2; and nxm is 1 or 2;

or geometrical and optical isomers thereof or their salts. Such compounds are exemplified by N-(1,2,5,6,7,8-hexahydro-5-methyl-2-oxo-5-quinolinyl)acetamide, 5-[[2-(3,4-dichlorophenyl)ethyl]amino]-5,6,7,8-tetrahydro-1-methyl-2(1H)-quinoline, and the like.

The above-mentioned compounds or salts thereof may be produced according to the process as described in JP-A 4-290872/1992 or its equivalent process.

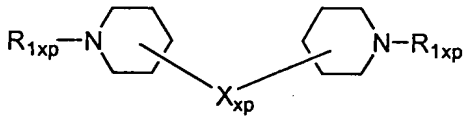
38) Compounds of the formula:



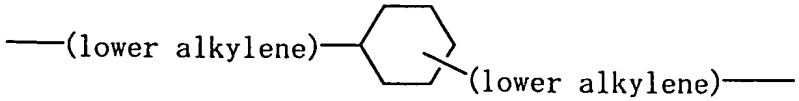
wherein R_{1xn}, R_{2xn} and R_{3xn} each is hydrogen, lower alkyl, lower alkoxy, hydroxy, halogen, nitro, cyano, amino optionally substituted by lower alkyl, or sulfamoyl optionally substituted by lower alkyl, or R_{1xn} and R_{2xn} taken together form methylenedioxy; R_{4xn} and R_{5xn} each is lower alkyl or cycloalkyl of 3 to 6 carbon atoms, or they taken together with the attached nitrogen atom may form 1-pyrrolidinyl, 1-piperidinyl, 1-piperazinyl or 4-morpholinyl, each of which may be substituted by lower alkyl; or salts thereof. Such compounds are exemplified by N-[4-[2- (dimethylamino)ethoxy]benzyl]-2-ethoxybenzamide, 4-amino-N-[4-[2-(dimethylamino)ethoxy]benzyl]-2-methoxy-5-sulfamoyl-benzamide, and the like.

The above-mentioned compounds or salts thereof may be produced according to the process as described in JP-A 2-231421/1990 or its equivalent process.

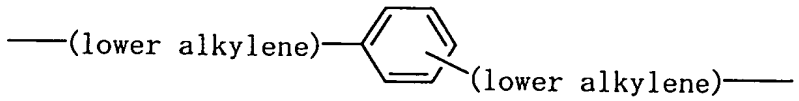
39) Compounds of the formula:



wherein Xxp is straight or branched chain alkylene of 1 - 10 carbon atoms or a group of the formula:



or of the formula:

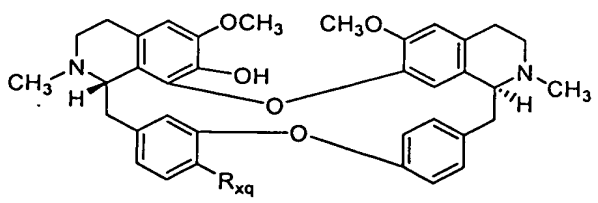


R_{1xp} is Arxp-CHR_{2xp} (where Arxp is unsubstituted phenyl or phenyl substituted by halogen, trifluoromethyl, lower alkyl or lower alkoxy; R_{2xp} is hydrogen or lower alkyl), cinnamyl of which the phenyl moiety is unsubstituted or substituted by halogen, lower alkyl or lower alkoxy, a cycloalkylmethyl, or methyl substituted by heterocyclic aromatic group; and when one linkage of X to the two piperidine rings is placed at the 2-position, the other is at the 2'-position, and when one is at the 3-position, the other is at the 3'-position, and when one is at the 4-position, the other is at the 4'-position;

or salts thereof. Such compounds are exemplified by 1,6-di-(1-benzyl-4-piperidyl)hexane, 1,5-di-(1-benzyl-4-piperidyl)- pentane, and the like.

The above-mentioned compounds or salts thereof may be produced according to the process as described in JP-A 4-18071/1992 or its equivalent process.

40) Compounds of the formula:

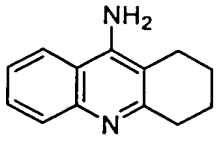


[wherein Rxq is hydroxy or methoxy]

or salts thereof.

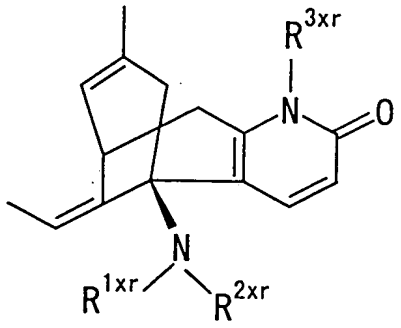
The above-mentioned compounds or salts thereof may be produced according to the process as described in JP-A 4-159225/1992 or its equivalent process.

41) 9-Amino-1,2,3,4-tetrahydroacridine represented by the following formula or salts thereof.



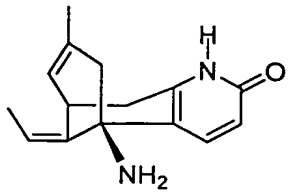
The above-mentioned compound or salts thereof may be produced according to the process as described in JP-A 4-346975/1992 or its equivalent process.

42) Compounds of the formula:



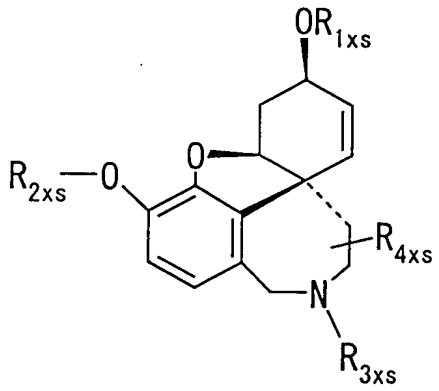
wherein R^{1xr}, R^{2xr} and R^{3xr} each is hydrogen or lower alkyl; or salts thereof.

Huperzine A represented by the following formula or salts thereof.



The above-mentioned compounds or salts thereof may be produced according to the process described in USP 5,177,082, J. Am. Chem. Soc., 1991, 113, p. 4695-4696, or J. Am. Chem. Soc., 1989, 111, p. 4116-4117, or its equivalent process, or obtained by extraction and isolation from a Chinese herb, Qian ceng ta (Lycopodium serratum (Huperizia serrata)Thunb).

43) Galanthamine or galanthamine derivatives represented by the following structural formula.

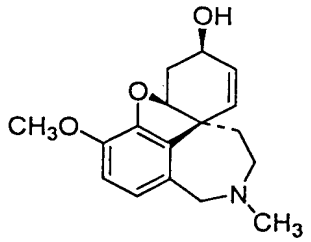


In the above formula, R_{1xs} and R_{2xs} are the same or different, each representing hydrogen or acyl such as lower alkanoyl, for example, acetyl, or a straight or branched alkyl, for example, methyl, ethyl, propyl, isopropyl, and the like.

R_{3xs} is straight or branched alkyl, alkenyl or alkaryl, and these groups may be replaced optionally by halogen, cycloalkyl, hydroxy, alkoxy, nitro, amino, aminoalkyl, acylamino, heteroaryl, heteroaryl-alkyl, aroyl, aroylalkyl, or cyano.

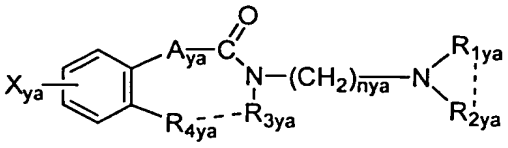
R_{4xs} means hydrogen or halogen attached to at least one of carbon atoms that constitute the tetra-cyclic skeletal structure; provided that when R_4 is placed at the adjacent position to the nitrogen atom, R_4 is preferably different from halogen, as well as from, for example, hydrohalides such as hydrobromide, hydrochloride, etc., methyl sulfate or methiodide.

Such a compound is exemplified by galanthamine represented by the following formula or salts thereof.



The above-mentioned compounds or salts thereof may be produced according to the process described in PCT JP-A 6-507617/1994, Heterocycles, 1977, 8, p. 277-282, or J. Chem. Soc. (C), 1971, p. 1043-1047, or its equivalent process, or obtained by extraction and isolation from a Liliaceae plant such as Galanthus nivalis or Galanthus waronowii.

44) Substituted amines of the formula:

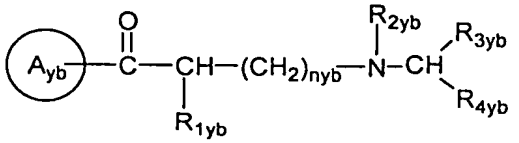


wherein R_{1ya} and R_{2ya} each is independently hydrogen or optionally substituted hydrocarbon residue, or they taken with the adjacent nitrogen atom form a heterocyclic group; as for R_{3ya} and R_{4ya}, R_{3ya} represents hydrogen or an optionally substituted hydrocarbon residue or acyl and R_{4ya} represents hydrogen, or R_{3ya} and R_{4ya} taken together may form $-(CH_2)_{mya}-$ CO-, $-CO-(CH_2)_{mya}-$ or $(CH_2)_{mya+1}-$ (where mya is 0, 1 or 2); A_{ya} represents $-(CH_2)_{lya}-$ (lya is 0, 1 or 2) or -CH=CH-; X_{ya} indicates 1 or more of substituents; nya is an integer of 4 to 7;

or salts thereof.

The above-mentioned compounds or salts thereof may be produced according to the process described in JP-A 2-91052/1990 or its equivalent process.

45) Aminoketone derivatives of the formula:

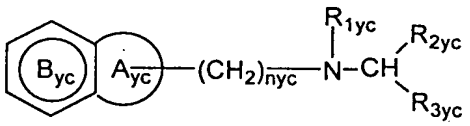


wherein the ring A_{yb} is a 5- to 8-membered cyclic group which may be substituted and may contain 1 or 2 ring-constituting heteroatoms of O, S and N; R_{1yb} is hydrogen or

optionally substituted hydrocarbon residue; R_{2yb} is hydrogen or lower alkyl; R_{3yb} is an optionally substituted aromatic group; R_{4yb} is hydrogen or lower alkyl or optionally substituted aromatic group; and nyb is an integer of 2 - 7; or salts thereof.

The above-mentioned compounds or salts thereof may be produced according to the process described in JP-A 3-95143/1991 or its equivalent process.

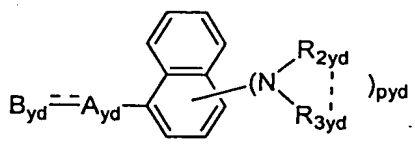
46) Aralkylamine derivatives of the formula:



wherein R_{1yc} is hydrogen or lower alkyl; R_{2yc} is an optionally substituted aromatic group; R_{3yc} is hydrogen or lower alkyl or optionally substituted aromatic group; nyc is an integer of 0 - 7; the ring A_{yc} is a 5- to 8-membered cyclic group which may be substituted and may contain 1 or 2 ring-constituting heteroatoms of O and S; the ring B_{yc} is an optionally substituted benzene ring;
or salts thereof.

The above-mentioned compounds or salts thereof may be produced according to the process described in JP-A 3-141244/1991 or its equivalent process.

47) Aminonaphthalene compounds of the formula:

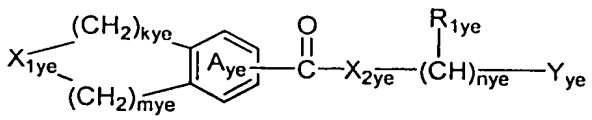


wherein B_{yd} is an optionally substituted saturated or unsaturated 5- to 7-membered aza-heterocyclic group; A_{yd} is a bonding or hydrocarbon residue, or bivalent or trivalent aliphatic hydrocarbon residue optionally substituted by oxo, hydroxyimino or hydroxy; --- indicates a single bond or double bond (provided that when A_{yd} is a bonding, then --- is a single bond), R_{2yd} and R_{3yd} each is independently hydrogen or optionally substituted hydrocarbon residue, or they taken with the adjacent nitrogen atom may form a cyclic amino; pyd is 1 or 2;

or salts thereof.

The above-mentioned compounds or salts thereof may be produced according to the process described in JP-A 3-223251/1991 or its equivalent process.

48) Condensed heterocyclic carboxylic acid derivatives of the formula:

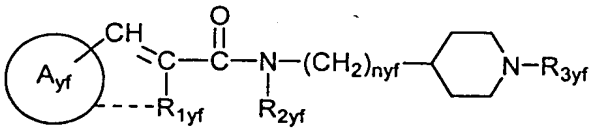


wherein X_{1ye} is R_{4ye}-N (R_{4ye} is hydrogen, optionally substituted hydrocarbon group or optionally substituted acyl), oxygen or sulfur; X_{2ye} is R_{5ye}-N (R_{5ye} is hydrogen, optionally substituted hydrocarbon group or optionally

substituted acyl) or oxygen; the ring A_{ye} is a benzene ring which may be substituted by an additional substituent; R_{1ye} is hydrogen or optionally substituted hydrocarbon group; each of R_{1ye} may be different according to repitition of nye; Y_{ye} is optionally substituted amino or optionally substituted nitrogen-containing saturated heterocyclic group; nye is an integer of 1 to 10; kye is an integer of 0 to 3; and mye is an integer of 1 to 8;
or salts thereof.

The above-mentioned compounds or salts thereof may be produced according to the process described in JP-A 5-239024/1993 or its equivalent process.

49) Unsaturated carboxylic amide derivatives of the formula:



wherein the ring A_{yf} is an optionally substituted aromatic ring; R_{1yf} is hydrogen or optionally substituted hydrocarbon residue, or it is taken with the adjacent group of -CH=C- and the two carbon atoms constituting the ring A_{yr} to form an optionally substituted carbocycle; R_{2yf} is hydrogen, or optionally substituted hydrocarbon residue or acyl; R_{3yf} is an optionally substituted hydrocarbon residue; and nyf is an integer of 2 to 6;

or salts thereof.

The above-mentioned compounds or salts thereof may be produced according to the process described in JP-A 2-138255/1990 or its equivalent process.

As for "non-carbamate-type amine compounds having an acetylcholinesterase inhibiting action" used in the invention, Compounds (I) are preferably exemplified.

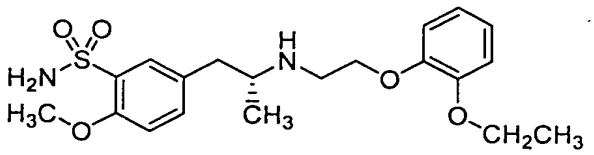
The non-carbamate-type amine compounds having an acetylcholinesterase inhibiting action used in the present invention, exhibit a potent effect increasing the contraction of the muscle of urinary bladder, with lesser toxicity, but not contracting the muscle of urethra. The compounds, accordingly, can be used as agents for improving excretory potency of the urinary bladder in mammals including human. The compounds can be used as prophylactic or therapeutic agents for dysuria, particularly for difficulty of urination, which is caused, for example, by the following items 1) to 6). 1) Prostatomegaly, 2) atresia in neck of urinary bladder, 3) neuropathic bladder, 4) diabetes mellitus, 5) surgical operation, and 6) hypotonia in muscle of urinary bladder. The compounds can also be used in treatment of dysuria such as pollakiuria, incontinence of urine, etc.

The non-carbamate-type amine compounds having an acetylcholinesterase inhibiting action, when used as

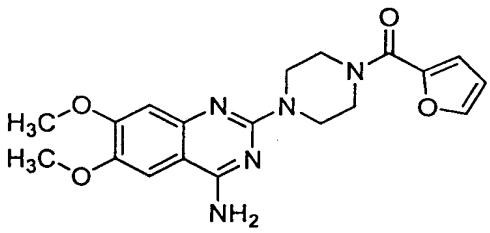
prophylactic and therapeutic agents in dysuria caused by prostatomegaly, particularly difficulty of urination, may be used in combination with other drugs (for example, α-blockers such as tamsulosin, and the like). These drugs may be used simultaneously or in combination of individually formulated preparations.

The α-blockers that can be used in combination with the compounds of the invention, include, for example, the following compounds or salts thereof.

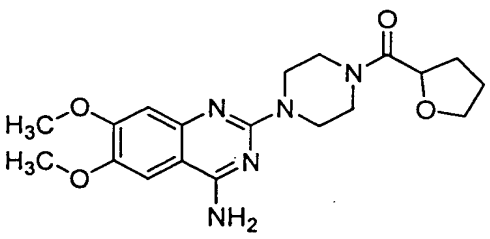
Tamsulosin: EP-A 34432, USP 4,703,063



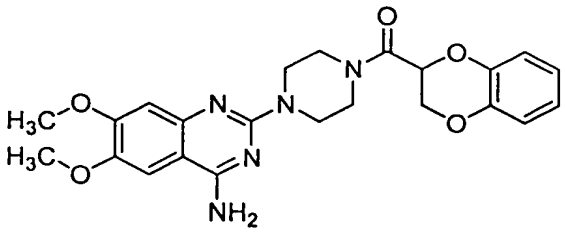
Prazosin: USP 3,511,836



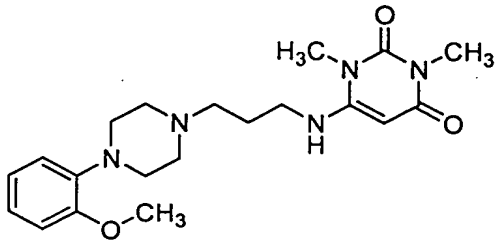
Terazosin: USP 4,026,894, USP 4,251,532



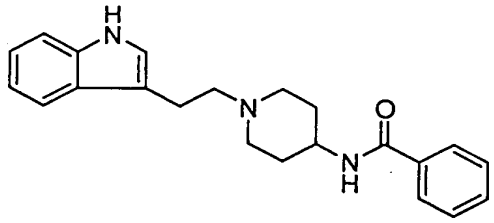
Doxazosin: USP 4,188,390



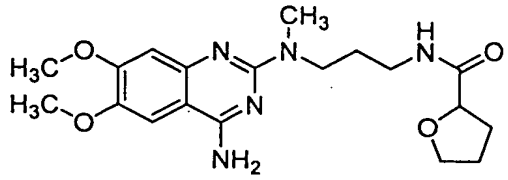
Urapidil: USP 3,957,786



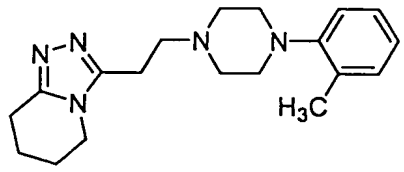
Indoramin: USP 3,527,761



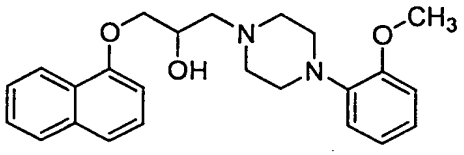
Alfuzosin: USP 4,315,007



Dapiprazole: USP 4,252,721

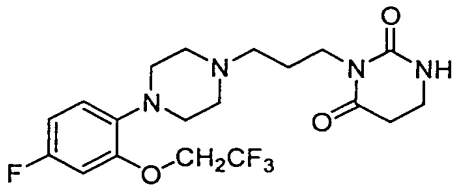


Naftopidil: USP 3,997,666

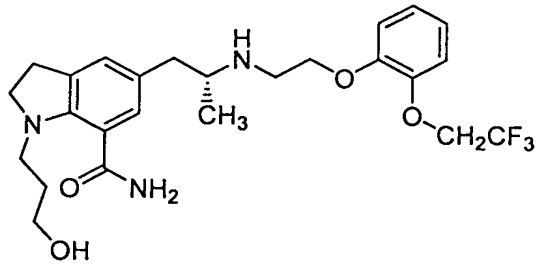


In addition, the following α-blockers are included.

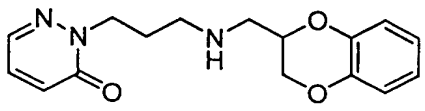
Ro 70-0004



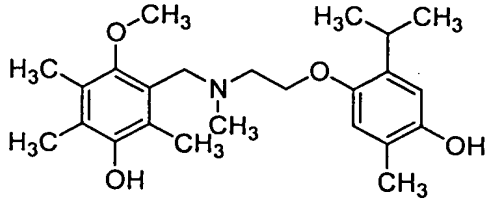
KMD-3213



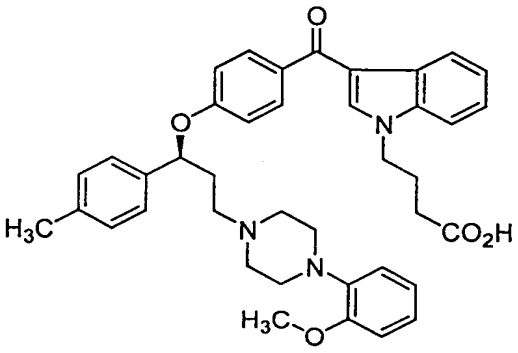
GYKI-16084



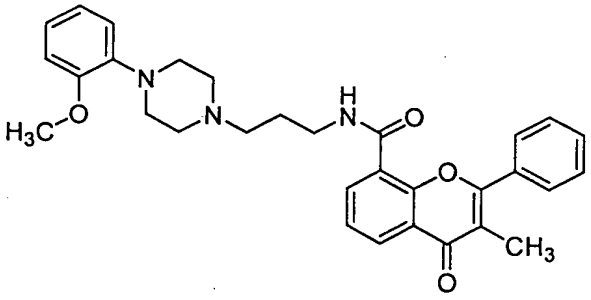
JTH-601



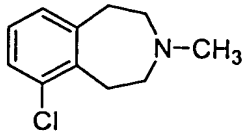
Z-350



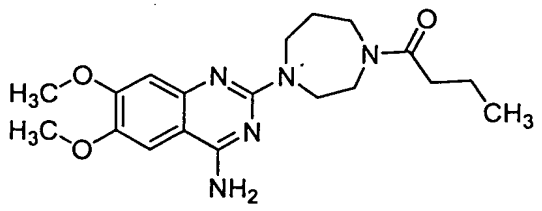
Rec-15-2739



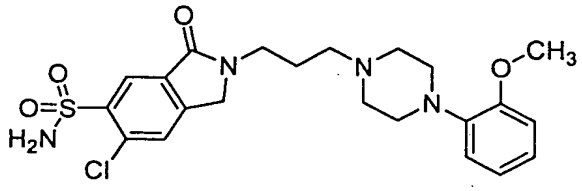
SK&F-86466



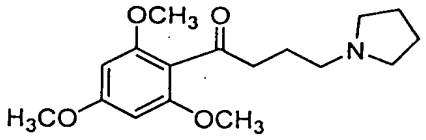
Bunazosin: USP 3,920,636



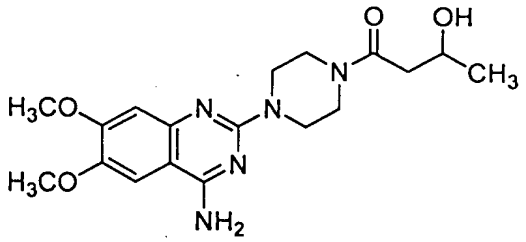
BMY-15037



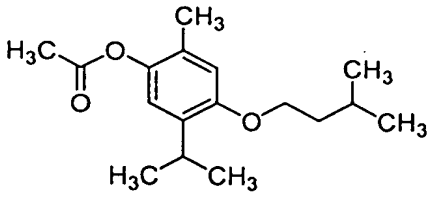
Buflomedil



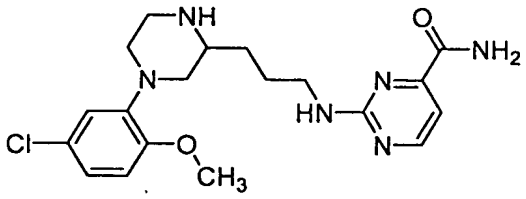
Neldazosin



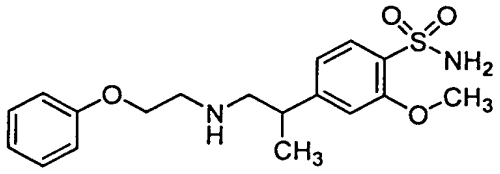
Moxisylyte



SL-890591



LY-23352



In addition, such α-blockers as ABT-980, AIO-8507-L, L-783308, L-780945, SL-910893, GI-231818, SK&F-106686, etc. are also included.

The non-carbamate-type amine compounds having an acetylcholinesterase inhibiting action used in the invention, can be formulated into pharmaceutical preparations according to the per se known methods. The compounds may be formulated into pharmaceutical compositions alone or with an appropriate amount of pharmacologically acceptable carriers by properly mixing in

a pharmaceutical process. Such pharmaceutical compositions include, for example, tablets (including sugar-coated tablets, film-coating tablets, etc.), powders, granules, capsules (including soft capsules), liquids and solutions, injections, suppositories, sustained release preparations; these preparations can safely be administered orally or parenterally (e.g., locally, rectally, intravenously, etc.).

In the agents for improving excretory potency of urinary bladder of the invention, the content of the non-carbamate-type amine compounds having an acetylcholinesterase-inhibiting action may be in about 0.1 - about 100% by weight for the total preparation. The agent, for example, as an agent for treating difficulty of urination, may be administered orally at a dose of about 0.005 - about 100 mg, preferably about 0.05 - about 30 mg, more preferably about 0.2 - about 10 mg, as an effective component for an adult (body weight: about 60 kg), though the dose is variable depending on the subject to be administered, route of administration, type of diseases, etc. This may be administered once a day or in several divided doses.

In the present invention, the pharmacologically acceptable carriers used in production of the agents for improving excretory potency of urinary bladder include a variety of organic or inorganic carrier materials

conventionally employed as pharmaceutical materials, for example, fillers, lubricants, binders, disintegrators, etc., for solid preparations, or solvents, solubilizing agents, suspending agents, tonicity adjusting agents, buffering agents, soothing agents, etc., for liquid preparations. If required, pharmaceutical additives such as preservatives, antioxidants, coloring agents, sweeteners, adsorbents, moistening agents, and the like may be added.

The fillers include, for example, lactose, refined sugar, D-mannitol, starch, corn starch, crystalline cellulose, light anhydrous silicic acid, and the like.

The lubricants include, for example, magnesium stearate, calcium stearate, talc, colloidal silica, and the like.

The binders include, for example, crystalline cellulose, refined sugar, D-mannitol, dextrin, hydroxypropyl cellulose, hydroxypropyl methyl cellulose, polyvinylpyrrolidone, starch, sucrose, gelatin, methylcellulose, sodium carboxymethylcellulose, and the like.

The disintegrators include, for example, starch, carboxymethyl cellulose, calcium carboxymethylcellulose, sodium carboxymethyl starch, L-hydroxypropyl cellulose, and the like.

The solvents include, for example, water for

injections, alcohol, propylene glycol, macrogol, sesame oil, corn oil, and the like.

The solubilizing agents include, for example, polyethylene glycol, propylene glycol, D-mannitol, benzyl benzoate, ethanol, trisaminomethane, cholesterol, triethanolamine, sodium carbonate, sodium citrate, and the like.

The suspending agents include, for example, surface activators such as stearyl triethanolamine, sodium laurylsulfate, laurylaminopropionic acid, lecithin, benzalkonium chloride, benzethonium chloride, glycerin monostearate, etc.; and hydrophilic high molecular materials such as polyvinyl alcohol, polyvinylpyrrolidone, sodium carboxymethylcellulose, methylcellulose, hydroxymethyl cellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, etc.

The tonicity adjusting agents include, for example, glucose, D-sorbitol, sodium chloride, glycerin, D-mannitol, and the like.

The buffering agents include, for example, buffer solutions of phosphate, acetate, carbonate, citrate, and the like.

The soothing agents include, for example, benzyl alcohol, and the like.

The preservatives include, for example,

paraoxybenzoic acid esters, chlorobutanol, benzyl alcohol, phenethyl alcohol, dehydroacetic acid, sorbic acid, and the like.

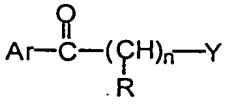
The anti-oxidants include, for example, sulfites, ascorbic acid, and the like.

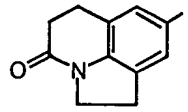
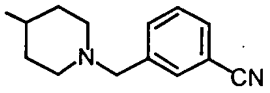
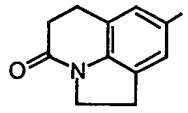
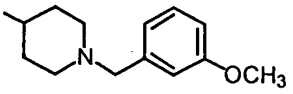
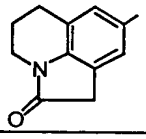
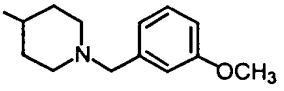
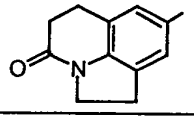
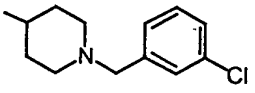
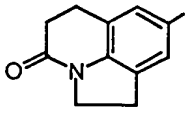
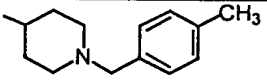
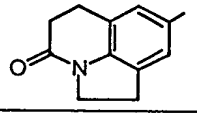
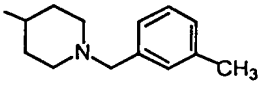
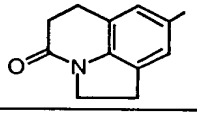
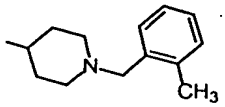
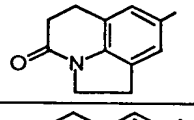
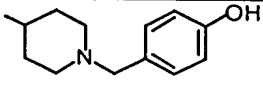
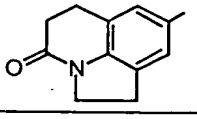
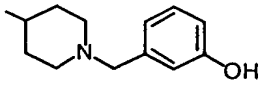
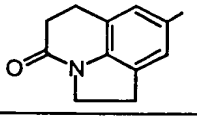
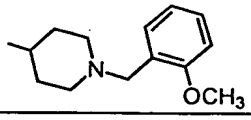
The invention will be explained in more detail based on the following Reference Examples, Examples, Experimental Examples, and Formulation Examples. These examples, however, are merely examples, and not intended to limit the invention. The invention may be modified as far as the modification does not depart from the scope of the invention.

Reference Examples 1 - 30

According to the per se known methods, compounds of Reference Examples 1 - 30 as depicted in the following Table were obtained.

[Table 1]



Reference Example No.	Ar	R	n	Y
1		H	2	
2		H	2	
3		H	2	
4		H	2	
5		H	2	
6		H	2	
7		H	2	
8		H	2	
9		H	2	
10		H	2	

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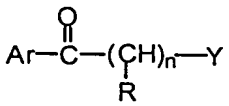
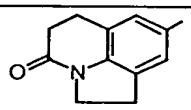
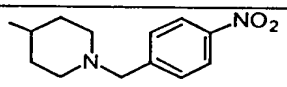
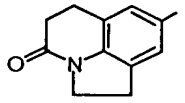
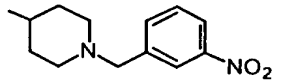
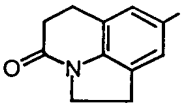
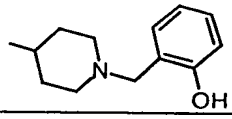
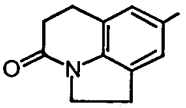
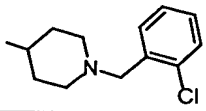
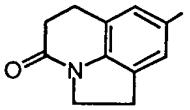
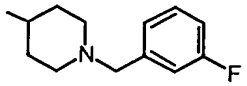
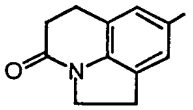
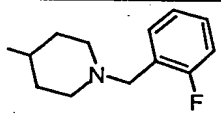
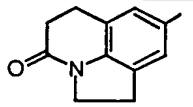
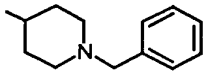
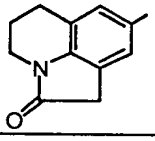
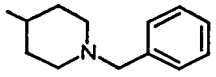
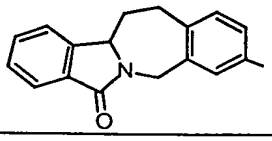
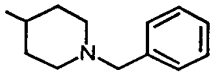
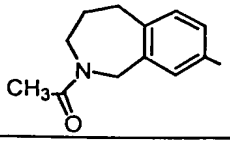
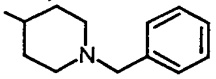
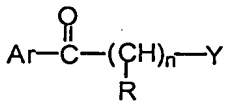
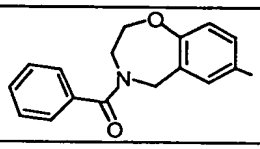
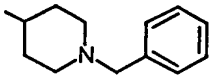
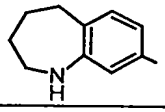
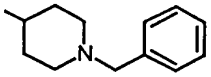
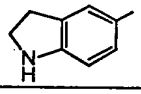
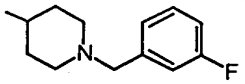
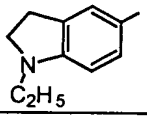
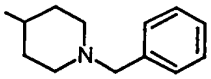
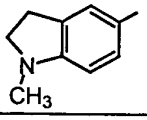
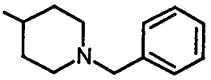
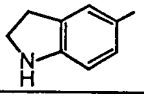
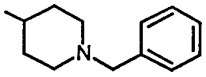
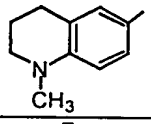
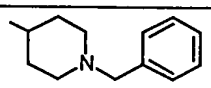
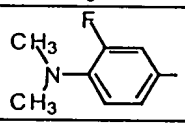
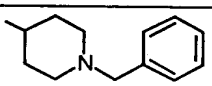


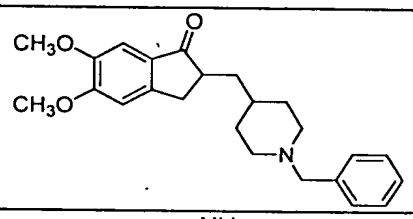
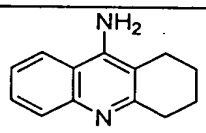
Reference Example No.	Ar	R	n	Y
11		H	2	
12		H	2	
13		H	2	
14		H	2	
15		H	2	
16		H	2	
17		H	2	
18		H	2	
19		H	2	
20		H	2	

[Table 3]



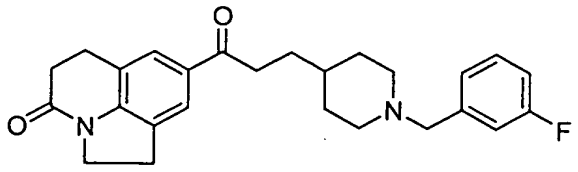
Reference Example No.	Ar	R	n	Y
21		H	2	
22		H	2	
23		H	2	
24		H	2	
25		H	2	
26		H	2	
27		H	2	
28		H	2	

[Table 4]

Reference Example No.	
29	
30	

Reference Example 15-1

8-[3-[1-[(3-fluorophenyl)methyl]-4-piperidinyl]-1-oxopropyl]-1,2,5,6-tetrahydro-4*H*-pyrrolo[3,2,1-*ij*]quinolin-4-one (Compound of Reference Example 15)



1) To thionyl chloride (300 mL) was added 3-(1-acetyl-4-piperidinyl)propionic acid (88.2 g, 0.443 mol) in small portions under ice cooling. The mixture was stirred at room temperature for 10 minutes, and then thionyl chloride was distilled off at 25°C under reduced pressure.

Diethyl ether was added to the residue and then evaporated in vacuo to give a yellow solid. Again, diethyl ether was added, and the solid was crushed with a spatula, and ether was evaporated in vacuo to give 3-(1-acetyl-4-piperidinyl)propionic acid chloride as crude light yellow powder. This light yellow powder and 1,2,5,6-tetrahydro-4*H*-pyrrolo[3,2,1-*ij*]quinolin-4-one (64.0 g, 0.369 mol) were suspended into 1,2-dichloroethane (200 mL), into which aluminum chloride (162 g, 1.21 mol) was added in small portions at room temperature. The mixture was stirred at room temperature for 12 hours, then added to ice-water, and extracted with ethyl acetate. The extract was washed with saturated brine, dried on anhydrous magnesium sulfate, and evaporated in vacuo to give a light yellow oily material. The oily material was purified by silica gel column chromatography (eluted with ethyl acetate/methanol=9 : 1) and crystallized from ethanol-diethyl ether to give 123.5 g of 8-[3-[(1-acetyl-4-piperidinyl)-1-oxopropyl]-1,2,5,6-tetrahydro-4*H*-pyrrolo[3,2,1-*ij*]quinolin-4-one as colourless crystals having mp. 157-159°C.

^{1}H-NMR ($CDCl_3$) δ 1.00-1.30 (2H, m), 1.50-1.95 (5H, m), 2.09 (3H, s), 2.53 (1H, dt, J=12.9, 2.4Hz), 2.72 (2H, t, J=7.6Hz), 2.90-3.15 (5H, m), 3.24 (2H, t, J=8.6Hz), 3.75-3.90 (1H, m), 4.14 (2H, t, J=8.6Hz), 4.55-4.70 (1H, m), 7.68 (1H, s), 7.73 (1H, s).

2) To 8-[3-[(1-acetyl-4-piperidinyl)-1-oxopropyl]-1,2,5,6-tetrahydro-4H-pyrrolo[3,2,1-ij]quinolin-4-one (118.7 g, 0.335 mol) obtained in 1) was added concentrated hydrochloric acid (600 mL), and the mixture was stirred at 140°C for 4 hours. After cooling to room temperature, hydrochloric acid was distilled off under reduced pressure, and the resulting residue was made basic (pH >12) with 8N-sodium hydroxide aqueous solution and extracted with ethyl acetate. The extract was washed with saturated brine, dried on anhydrous sodium sulfate, evaporated in vacuo, and crystallized from ethyl acetate-diethyl ether to give 103.7 g of 8-[3-[(4-piperidinyl)-1-oxopropyl]-1,2,5,6-tetrahydro-4*H*-pyrrolo[3,2,1-*ij*]quinolin-4-one as colourless crystals having mp. 114-115°C. ^{1}H-NMR ($CDCl_3$) δ 1.00-1.30 (2H, m), 1.30-1.90 (7H, m), 2.59 (2H, dt, J=12.0, 2.4Hz), 2.72 (2H, t, J=7.6Hz), 2.85-3.15 (5H, m), 3.23 (2H, t, J=8.6Hz), 4.14 (2H, t, J=8.6Hz), 7.68 (1H, s), 7.73 (1H, s).

3) To a solution of 8-[3-[(4-piperidinyl)-1-oxopropyl]-1,2,5,6-tetrahydro-4*H*-pyrrolo[3,2,1-*ij*]quinolin-4-one (103.7 g, 0.332 mol)(obtained in 2)) in acetonitrile (750 mL) was added 3-fluorobenzyl bromide (65.9 g, 0.349 mol) and anhydrous potassium carbonate (80 g), and the mixture was stirred at room temperature for 12 hours. The reaction mixture was added to a mixture of ethyl acetate

and water, and the organic layer was separated. The organic layer was washed with saturated brine, dried on anhydrous magnesium sulfate, and concentrated to give a light yellow oily material. The oily material was purified by silica gel column chromatography (eluted with ethyl acetate/methanol=9 : 1). The resulting crude crystals were recrystallized from hot ethanol to give the title compound (111.2 g) as colourless crystals having mp. 111-112°C.

^{1}H-NMR ($CDCl_3$) δ 1.20-1.50 (4H, m), 1.55-1.80 (4H, m), 1.85-2.05 (2H, m), 2.71 (2H, t, J=7.6Hz), 2.80-3.15 (5H, m), 3.22 (2H, t, J=8.6Hz), 3.47 (2H, s), 4.13 (2H, t, J=8.6Hz), 6.85-7.15 (3H, m), 7.20-7.35 (1H, m), 7.67 (1H, s), 7.72 (1H, s).

Elemental analysis for $C_{26}H_{29}FN_2O_2$:

Calcd: C, 74.26; H, 6.95; N, 6.66

Found: C, 74.28; H, 7.02; N, 6.58

The above-mentioned title compound (65.4 g) was dissolved in ethanol, to which was added 1.5 equivalent of 4N-hydrochloric acid (ethyl acetate solution). The solvent and excess hydrochloric acid were distilled off to give colourless powder, which was crystallized from ethanol to give 64.1 g of the hydrochloride of title compound as colourless crystals having mp. 201-203°C (dec.).

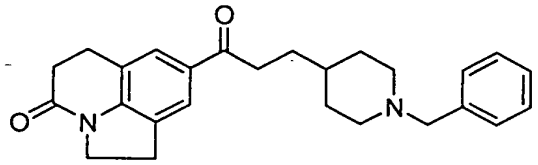
Elemental analysis for $C_{26}H_{29}FN_2O_2 \cdot HCl$:

Calcd: C, 68.34; H, 6.62; N, 6.13

Found: C, 68.15; H, 6.66; N, 6.04

Reference Example 15-2

8-[3-[1-(phenylmethyl)-4-piperidinyl]-1-oxopropyl]-1,2,5,6-tetrahydro-4*H*-pyrrolo[3,2,1-*ij*]quinolin-4-one (Compound of Reference Example 17)



8-[3-[(4-Piperidinyl)-1-oxopropyl]-1,2,5,6-tetrahydro-4H-pyrrolo[3,2,1-ij]quinolin-4-one [obtained in section 2) of Reference Example 15-1 and benzyl bromide were treated in the same manner as in section 3) of Reference Example 15-1 to give colourless powder, which was crystallized from ether-isopropyl ether to give the title compound as colourless crystals having mp. 103-104°C.

^{1}H-NMR ($CDCl_3$) δ 1.20-1.75 (8H, m), 1.85-2.05 (2H, m), 2.71 (2H, t, J=7.6Hz), 2.80-2.95 (3H, m), 3.02 (2H, t, J=7.6Hz), 3.22 (2H, t, J=8.6Hz), 3.49 (2H, s), 4.13 (2H, t, J=8.6Hz), 7.20-7.35 (5H, m), 7.67 (1H, s), 7.71 (1H, s).

Elemental analysis for $C_{26}H_{30}N_2O_2$:

Calcd: C, 77.58; H, 7.51; N, 6.96

Found: C, 77.30; H, 7.49; N, 7.20

The above-mentioned title compound was dissolved in ethanol, to which was added 1.5 equivalent of 4N-

hydrochloric acid (ethyl acetate solution). The solvent and excess hydrochloric acid were distilled off to give colourless powder, which was crystallized from ethanol to give the hydrochloride of title compound as colourless crystals having mp. 245-248°C (dec.).

Elemental analysis for $C_{26}H_{30}N_2O_2 \cdot HCl$:

Calcd: C, 71.14; H, 7.12; N, 6.38

Found: C, 70.97; H, 7.14; N, 6.18

Formulation Example 1

Hereinafter, the hydrochloride of Compound of Reference Example 15 (8-[3-[1-[(3-fluorophenyl)methyl]-4-piperidinyl]- 1-oxopropyl]-1,2,5,6-tetrahydro-4H-pyrrolo[3,2,1-ij]-quinolin-4-one) is abbreviated to Compound A.

(1)	Compound A	1g
(2)	Lactose	197 g
(3)	Corn starch	50 g
(4)	Magnesium stearate	2 g

The above components (1), (2) and corn starch (20 g) were mixed, and formulated into granules with a paste prepared from corn starch (15 g) and 25 mL of water. Corn starch (15 g) and the above component (4) were added thereto, and the mixture was compressed with a compressed tablet machine to give 2000 tablets of 3 mm in diameter containing 0.5 mg/tablet of Compound A.

Formulation Example 2

(1)	Compound A	2g
(2)	Lactose	197 g
(3)	Corn starch	50 g
(4)	Magnesium stearate	2 g

According to the same manner as in Formulation Example 1, 2000 tablets of 3 mm in diameter containing 1.0 mg/tablet of Compound A were produced.

Formulation Example 3

(1)	Compound A	5.0 mg
(2)	Lactose	60.0 mg
(3)	Corn starch	35.0 mg
(4)	gelatin	3.0 mg
(5)	Magnesium stearate	2.0 mg

A mixture of the above components (1), (2) and (3) together with 0.03 ml of 10% gelatin aqueous solution (3.0mg of gelation) was passed through a 1 mm mesh sieve to form granules, which were dried at 40°C and again sieved. The resulting granules were mixed with the above component (5) and compressed. The resulting core tablets were sugar-coated with an aqueous coating suspension containing sucrose, titanium dioxide, talc and gum arabic. The coated tablets were polished with yellow beeswax to give final coated tablets.

Experimental Example 1

Measurement of acetylcholinesterase-inhibiting action

Acetylcholinesterase-inhibiting action of the compounds disclosed in Reference Examples was measured using acetylcholinesterase of human erythrocyte origin according to the acetylthiocholine method (Ellman method).

Acetylcholinesterase of human erythrocyte origin (Sigma Chemical Co.) was dissolved in distilled water at a concentration of 0.2 IU/mL to give an enzyme authentic sample. To a 96-well microplate was dispensed 20μL of drug solution, 30μL of 80mM Tris-HCl (pH 7.4), 50μL of enzyme authentic sample and 50μL of 5mM 5,5-dithio-bis(2-nitrobenzoic acid)(Sigma Chemical Co.), and the plate was shaken for 10 seconds. Then, 50μL of acetylthiocholine iodide (Sigma Chemical Co.) was added, and the plate was again shaken. Immediately after shaking, increase of extinction at 414 nM was measured at intervals of 30 seconds for 10 minutes. The enzyme activity was determined according to the following equation.

$$R = 5.74 \times 10^{-7} \times \Delta_A$$

(wherein R indicates an enzyme activity (mol), and Δ_A shows increase of extinction at 414 nM)

The experiment was repeated at least 3 times for each compound to obtain 50% inhibitory concentration (IC_{50}). Moreover, in the same manner as mentioned above, acetylcholinesterase-inhibiting activity of distigmine was

measured. The following table shows the result.

[Table 5]

Compd. No. in Reference Example (Salt)	IC_{50} (nM)
1 (Hydrochloride)	13.6
4 (Hydrochloride)	10.9
6 (Hydrochloride)	18.9
7 (Hydrochloride)	22.1
12 (Hydrochloride)	8.1
13 (Hydrochloride)	5.2
14 (Hydrochloride)	9.9
15 (Hydrochloride)	4.4
17 (Hydrochloride)	7.8
18 (Hydrochloride)	10.9
Distigmine	723.3

From the above results, it is found that Compounds (I) exhibit a potent acetylcholinesterase-inhibiting action.

Experimental Example 2

Potentiation effect of the compounds disclosed in Reference Examples for rhythmic contraction of urinary bladder in guinea pig

Potentiation effect of the compounds disclosed in Reference Examples for rhythmic contraction of urinary bladder was examined using Hartley male guinea pigs. Hartley male guinea pigs (SLC) weighing about 300 g were anesthetized with urethane (1.2 g/kg, i.p.), held, and

incised at the midline of abdomen to expose the bladder. The urethra was ligated, and a polyethylene tube (PE-50) was inserted into the bladder. The internal pressure of the bladder was measured with a blood pressure amplifier (Nippon Koden), and the data was collected on a personal computer through an A/D converter (MP-30, Biopac Systems). A proper amount of physiological saline was injected into the bladder through a cannula to induce rhythmic contraction of the bladder. To the animals in which occurrence of stable rhythmic contraction was confirmed at a rate of 1 time every 2 minutes to 10 minutes, a solution of the test compound dissolved in distilled water was injected intravenously, and the effect was observed.

The data was manipulated according to the following process.

The area (AUC) that is formed by a curve of the internal pressure of the bladder and a base line was calculated through analytical software (Studentlab pro 2.1.5, Biopac Systems) to evaluate the effect of the test compounds. The curve of the internal pressure is made based on the bladder contraction immediately before administration of the test compound and the first contraction 5 minutes after the administration. From the dose-dependent curve of AUC, the dose at which AUC before drug administration was increased 2 times (AUC200) was

calculated to determine potency of contraction-enhancing effect of the test compounds for the muscle of urinary bladder. In addition, the potency of contraction-enhancing effect of stigmine for the muscle of bladder was determined in the same manner as mentioned above.

The following table shows the AUC200 values of each compound.

[Table 6]

Compd. No. in Reference Example (Salt)	AUC200 (mg/kg, i.v.)
1 (Hydrochloride)	0.005
2 (Hydrochloride)	0.059
3 (Hydrochloride)	0.14
4 (Hydrochloride)	0.005
5 (Hydrochloride)	0.06
6 (Hydrochloride)	0.0049
7 (Hydrochloride)	0.0055
8 (Hydrochloride)	0.076
9 (Hydrochloride)	0.027
10 (Hydrochloride)	0.031
11 (Hydrochloride)	0.12
12 (Hydrochloride)	0.006
13 (Hydrochloride)	0.0013
14 (Hydrochloride)	0.0016
15 (Hydrochloride)	0.0013
16 (Hydrochloride)	0.015
17 (Hydrochloride)	0.0034
18 (Hydrochloride)	0.0051
19 (Hydrochloride)	0.065
20 (Hydrochloride)	0.065
21 (Hydrochloride)	0.19
22 (Fumarate)	0.16
23 (Fumarate)	0.073
24 (Fumarate)	0.18
25 (Fumarate)	0.13
26 (Fumarate)	0.082

27 (Fumarate)	0.1
28 (Fumarate)	0.16
29 (Hydrochloride)	0.16
Distigmine	0.1

From the above results, it is found that Compounds (I) exhibit a high potentiation effect for rhythmic contraction of urinary bladder.

Experimental Example 3

Effect on urination efficiency in guinea pigs

Effect of the compounds of Reference Examples on urination efficiency was examined using Hartley male guinea pigs. Six to ten Hartley male guinea pigs weighing 346.5±3.5 g (SLC) were employed in each treated group. Guinea pigs were anesthetized with urethane, and held, and the bladder was exposed. Two polyethylene tubes (PE-50 and PE-100) were inserted into the bladder. One (PE-50) of the tubes was used in infusion of physiological saline, and the other (PE-100) was used for measurement of the internal pressure of the bladder. Saline was infused continuously at a flow rate of 0.3 mL/min. The infusion was stopped at the time when intermittent urination was confirmed at least 3 times, and the whole saline in bladder was removed. Again, infusion was started, and stopped at the time when a rise of the pressure in bladder was confirmed immediately before urination, and the time required for infusion and

the weight of excreted urine were measured. Efficiency of urination was calculated from the following equation.

Efficiency of urination(%) =

100 X Excreted volume (mL)/Infusion time (min) X 0.3 (mL/min)

Measurement was made at least 2 times before administration of the test compound, and then the test compound was dissolved in distilled water and administered intravenously. As for distigmine, the value was measured 30 minutes after administration, and as for the compounds of Reference Examples, the measurement was made 10 minutes after administration. Effect by administration of solvents was also confirmed.

The average measured value before administration of the test compounds was regarded as the value before administration, and applied to the paired-t test for a significant difference test with the value after the administration. (** $p<0.01$, * $p<0.05$)

The following table shows the effect on efficiency of urination.

[Table 7]

Compound	Dose (mg/kg)	Efficiency of Urination(%)		Improvement of Efficiency (%)
		Before adm.	After adm.	
Vehicle	-	77.4±6.4	78.4±6.5	2.4
Distigmine	0.1	79.1±5.7	90.9±2.7	20.4
Distigmine	0.3	67.4±4.3	75.3±3.7	14.7
Distigmine	1	78.6±6.7	67.8±4.6	-11.6

Distigmine	3	68.6±7.0	48.1±8.5	-30.9**
Vehicle	-	77.4±6.4	82.8±4.7	12.9
Compd. of Ref. Ex. 15	0.003	71.5±7.9	79.6±6.4	16.2
Compd. of Ref. Ex. 15	0.01	60.0±7.7	93.9±3.0	77.0**
Compd. of Ref. Ex. 15	0.03	65.5±9.0	88.9±3.1	66.2*
Vehicle	-	78.5±6.0	73.7±8.9	-7.1
Compd. of Ref. Ex. 30	0.3	62.2±5.1	74.5±5.1	22.0**
Compd. of Ref. Ex. 30	1.0	62.8±7.8	84.9±4.8	55.4*
Compd. of Ref. Ex. 30	3.0	65.8±8.9	89.0±2.7	64.2*

** $p<0.01$, * $p<0.05$

From the above results, it is found that improvement of urination efficiency by distigmine is poor and it makes the efficiency worse at a high dose, while Compounds (I) improve the efficiency greatly and significantly, and do not make the efficiency worse even at high doses.

Experimental Example 4

Effect on the flow rate of urine in guinea pigs

Effect on the flow rate of urine by single or combined use of Compounds of Reference Examples, distigmine, prazosin, and tamsulosin was examined using Hartley male guinea pigs. Four to six Hartley male guinea pigs weighing about 350 g (SLC) were employed in each treated group. Guinea pigs were anesthetized with urethane, and held, and the bladder was exposed. Two polyethylene tubes (PE-100) were inserted into the bladder. One of the tubes was used

in infusion of physiological saline, and the other used for measurement of the internal pressure of the bladder. Saline was infused continuously at a flow rate of 0.3 mL/min. The infusion was stopped at the time when intermittent urination was confirmed at least 3 times, and the whole saline in bladder was removed. Again, infusion was started, and stopped at the time when a rise of the pressure in bladder was confirmed immediately before urination. Excreted urine was weighed on an electronic force balance (HX-400, A&D). Analogue data of the internal pressure of the bladder and urine weight were input in an AD converter (MP-30, Biopac Systems) and the digital signal was analyzed by means of purpose-made software (Student lab pro 2.1.5, Biopac Systems). Sampling interval of the date was fixed at 0.1 second, and the value of urine weight was differentiated to determine the flow rate of urine. In order to remove data noise of the excretion volume and flow rate of urine, the data was adapted to a lowcut filter at 0.5Hz.

Measurement was made 2 times before administration of the test compound, and then the test compound was administered intravenously. Again, measurement was made 10 minutes after administration of the test compound. Effect by administration of solvents was also confirmed as a control experiment.

The average measured value before administration of the test compounds was regarded as the value before administration, and the rate of change of the values from the ante-administration to the post-administration was calculated to compare between the groups by means of the Dunnet's test.

Effect on the flow rate of urine is summarized in the following table.

[Table 8]

	Dose (mg/kg)	n	Flow Rate (mL/sec) Ante-admn.	Post-admn.	Improvement (%)
DMSO (Control)	-	5	0.34±0.05	0.30±0.05	-13.85±6.48
Prazosin	0.1	5	0.18±0.03	0.17±0.02	0.97±10.32
Distigmine	1.0	6	0.25±0.05	0.22±0.05	-8.31±11.13
Distigmine + Prazosin	1.0 0.1	4	0.30±0.07	0.25±0.09	-24.17±12.31
Compd. of Ref. Ex.15	0.01	5	0.27±0.03	0.29±0.05	6.81±7.84
Compd. of Ref. Ex.15 + Prazosin	0.01 0.1	5	0.18±0.01	0.25±0.03	42.37±15.25**

** $p<0.01$ vs DMSO (Control)

[Table 9]

	Dose (mg/kg)		Flow Rate (mL/sec) Ante-admn.	Post-admn.	Improvement (%)
Distilled Water (Control)	-	11	0.16±0.01	0.12±0.01	-22.0±6.5
Tamsulosin	0.1	11	0.16±0.01	0.14±0.02	-11.8±4.8

Compd.of Ref. Ex.15	0.001	9	0.17±0.03	0.15±0.02	-6.5±12.1
Compd.of Ref. Ex.15 +Tamsulosin	0.001 0.1	10	0.15±0.01	0.16±0.01	11.3±9.2*

* $p<0.05$ vs distilled water (Control)

From the above result, it is found that improvement of the flow rate of urine by distigmine alone is poor and not enhanced even in combination with an α-blocker prazosin. On the other hand, it is recognized that Compound (I) per se improves the flow rate of urine, which is further increased considerably in combination with α-blockers, prazosin and tamsulosin.

From the result of the above-mentioned Experimental Examples 2, 3 and 4, it is found that non-carbamate-type amine compounds showing an acetylcholinesterase-inhibiting action, particularly, Compounds (I) have a potent effect for improving excretory potency of the urinary bladder.

Industrial Applicability

The amine compounds used in the present invention show a high effect increasing the contraction potency of the muscle of urinary bladder but no effect of contracting the muscle of urethra. They are, accordingly, useful as

agents for improving excretory potency of the urinary bladder with high efficiency of urination. In addition, they are useful as prophylactic or therapeutic agents for dysuria, particularly for difficulty of urination.